

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
12 July 2001 (12.07.2001)

PCT

(10) International Publication Number  
**WO 01/49721 A2**

(51) International Patent Classification<sup>7</sup>: **C07K 14/195**,  
C12N 15/31, G01N 33/68, C12Q 1/68, A61K 48/00,  
38/16, G01N 33/50

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(21) International Application Number: PCT/US00/35604

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(22) International Filing Date:  
29 December 2000 (29.12.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/174,089 30 December 1999 (30.12.1999) US

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(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ,  
DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,  
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,  
TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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Published:

— Without international search report and to be republished  
upon receipt of that report.

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.

WO 01/49721 A2

(54) Title: NOVEL BACTERIAL GENES AND PROTEINS THAT ARE ESSENTIAL FOR CELL VIABILITY AND THEIR  
USES

(57) Abstract: The present invention provides novel bacterial genes and their encoded polypeptides thereof which are essential for  
bacterial cell viability, and their uses.

## NOVEL BACTERIAL GENES AND PROTEINS THAT ARE ESSENTIAL FOR CELL VIABILITY AND THEIR USES

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10 Throughout this application various publications are referenced. The disclosures of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

### FIELD OF THE INVENTION

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The present invention relates generally to nucleotide sequences, and polypeptides encoded by the sequences, that are essential for bacterial viability, and to methods of using the nucleotide and polypeptide sequences.

### 20 BACKGROUND OF THE INVENTION

Bacterial genera, such as *Streptococcus*, *Staphylococcus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Enterobacter*, are the cause of numerous afflictions in humans and animals. Bacterial infection can lead to serious health conditions, including pneumonia,  
25 osteomyelitis, meningitis, sinusitis, otitis, cystitis, and even food poisoning. Typically, these infections can be treated with standard antimicrobial agents such as antibiotics. However, the emergence of pathogenic bacterial strains that are resistant to antibiotics has risen alarmingly in the past two decades. This situation has created an urgent need for the development of new antimicrobial agents.

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One strategy for developing new antimicrobial agents is to identify bacterial gene sequences that encode gene products that are essential for bacterial cell viability and

develop and/or identify agents which inhibit the function of the gene product. DNA sequencing technology has advanced from sequencing one gene at a time to sequencing entire genomes, the sum of all genes in an organism. With the recent arrival of bacterial genomic information, it is now possible to compare multiple bacterial genomes in an attempt to identify genes that encode conserved gene products. In this manner, one skilled in the art may identify a set of conserved bacterial genes, including a subset of genes that are essential for bacterial cell viability. The essential gene is then used as a starting point to develop therapeutic agents that inhibit or inactivate the product of the essential gene.

The availability of DNA sequence information for multiple microbial genomes is a recent development. The public release of the first complete genome, *Haemophilus influenzae* (Fleischmann, R.D., et al. 1995 *Science* 269:496-512 ), was followed in rapid succession by a number of public and private genome sequencing programs. Presently, some 20 completely sequenced bacterial genomes have been published, and over 100 other sequencing projects are underway (Blattner, F.R., et al., 1997 *Science* 277:1453-74; Ferretti, J.J., et al., 1997 *Adv Exp Med Biol* 418:961-963; Koonin, E.V., et al., 1996 *Methods Enzymol* 266:295-322). Analyses of these data indicate that approximately 46% of putative bacterial genes are of unknown function having no attributable function.

Others have pursued various strategies to identify bacterial genes that are essential for viability. These strategies include: identifying genes that are expressed by the bacteria when present in the infected host (Hensel, M., et al., 1995 *Science* 269:400-3), identifying essential genes by isolating temperature sensitive mutants (Schmid, M.B., et al., 1998 *Curr Opin Chem Biol* 2:529-34), and identifying genes in pathways known from prior physiological studies to be essential (Skarzynski, T. et al., 1996 *Structure* 1996 4:1465-74)

There continues to be a need to identify bacterial genes that encode gene products that are essential for cell viability, such as cell replication, growth, and survival. These genes and their encoded gene products can be used as a starting point towards identifying agents

that inhibit functions essential for cell viability, thereby causing bacterial cell stasis or death (e.g., antibacterial agents).

5 The present invention provides experimental identification of novel, conserved essential genes (*ceg*) from bacteria and their encoded protein products. The *ceg* genes are considered essential to cell viability because disruption of an endogenous *ceg* gene results in lethality of a bacterial cell (e.g., as determined by failure to recover viable chloramphenicol-resistant colonies, as described herein). Thus, the gene products encoded by these genes are potentially valuable targets for chemotherapeutic intervention  
10 of bacterial infections.

The *ceg* nucleotide sequences of the invention were obtained by large-scale computational comparisons of multiple genome sequences to identify conserved protein coding regions, followed by gene disruption to identify *cegs*. The conservation of protein  
15 sequences in many cases is believed to reflect the higher level conservation of common biochemical pathways essential for bacterial function and viability.

#### SUMMARY OF THE INVENTION

20 The acronyms "CEG" and "*ceg*" stand for Conserved Essential Gene. For convenience, the italicized term *ceg* refers herein to *ceg* nucleotide sequences. The capitalized term CEG refers herein to CEG polypeptide sequences.

Embodiments of the *ceg* nucleotide sequences and the CEG polypeptide sequences are  
25 designated CFEs which stands for CEG For Expression. The CFEs are polypeptides resulting from expression of the *ceg* nucleotide sequence.

The present invention provides isolated nucleotide sequences of conserved essential genes from bacteria, designated *ceg*. The invention also provides recombinant nucleic  
30 acid molecules including the *ceg* sequences of the invention, and methods of uses thereof. Examples of nucleic acid molecules having *ceg* sequences are described in SEQ ID



NOS.: 1-113. The invention further provides isolated polypeptides and recombinant polypeptides having the CEG sequences of the invention, and methods of uses thereof. Examples of polypeptides having CEG sequences are described in SEQ ID NOS.:114-226.

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The *ceg* sequences of the present invention are DNA or RNA. Further, the invention includes nucleic acid molecules that are identical or nearly identical (e.g., similar) with the *ceg* sequences of the invention. The invention additionally provides polynucleotide sequences that hybridize under stringent conditions to the *ceg* sequences of the invention.

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A further embodiment provides polynucleotide sequences which are complementary to the *ceg* sequences of the invention. Yet another embodiment provides *ceg* nucleic acid molecules that are labeled with a detectable marker. Another embodiment provides recombinant nucleic acid molecules, such as a vector or a fusion molecule, including the *ceg* sequences of the invention.

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The present invention provides various *ceg* sequences, fragments thereof having essential gene activity, and related molecules such as antisense molecules, oligonucleotides, peptide nucleic acids (PNA), fragments, and portions thereof.

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The present invention relates to the inclusion of the polynucleotides encoding CEG gene products, such as CEG polypeptides, in an expression vector which can be used to transform host cells or organisms. Such transgenic hosts are useful for the production of CEG gene products for the development of antibacterial agents such as antibiotics.

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The invention further provides substantially purified CEG gene products, and uses thereof.

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The invention also relates to pharmaceutical compositions comprising antisense molecules capable of disrupting expression of *ceg* sequences, agonists, antagonists or inhibitors of CEG gene products, and antibodies reactive against the CEG polypeptides.

These compositions are useful for preventing the growth or survival of bacteria, for example, in the treatment of conditions associated with bacterial infections.

### **BRIEF DESCRIPTION OF THE FIGURES**

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Figure 1: A schematic representation of the gene disruption assay, as described in Example 3, *infra*. A) A recombinant vector undergoing homologous recombination with the host genome. B) The result of homologous recombination.

- 10 Figure 2: A schematic representation of the polarity test for operons, as described in Examples 2 and 3, *infra*. A) The recombinant vector undergoing homologous recombination with the host genome. B) Case 1: one possible result of homologous recombination; the downstream Gene B has an independent promoter. C) Case 2; another possible result of homologous recombination; the downstream Gene B does not have an
- 15 independent promoter.

- Figure 3: Purification of 2CFE 75, as described in Example 6, *infra*. A) Fractionation profile of 2CFE 75 eluted from a Ni-NTA column. B) Gel electrophoresis of pooled fractions of CFE 75. C) Non-denaturing gel electrophoresis to determine oligo form of
- 20 2CFE 75.

Figure 4: Fractionation profile of 2CFE 3 eluted from a hydroxyapatite column, as described in Example 7, *infra*.

- 25 Figure 5: The biosynthesis pathway of Coenzyme A which starts with phosphorylation of pantothenate.

- Figure 6: Circular dichroism spectra of 2CFE 101 and 103, as described in Example 10, *infra*. A) Circular dichroism spectra of 2CFE 101 and 103 at 25 degrees C. B) Circular
- 30 dichroism thermal melt spectra of 2CFE 101 and 103 at a range of zero to 100 degrees C.

Figure 7: Circular dichroism spectra of aggregate and monomer pools of 2CFE 101 and 103, as described in Example 10, *infra*. A) Circular dichroism spectra of aggregate and monomer pools of 2CFE 101 and 103 at 25 degrees C. B) Circular dichroism thermal melt spectra of aggregate and monomer pools of 2CFE 101 and 103 at a range of zero to 100 degrees C.

5

Figure 8: Absorbance spectra of pantothenate-dependent production of ADP, as described in Example 10, *infra*.

Figure 9: The results of size exclusion chromatography and gel electrophoresis showing the oligomeric forms of 2CFE 21 and 39, as described in Example 11, *infra*. Lanes 1-6 contain 2CFE 21, lane 7 is a molecular weight marker, lanes 8-10 contain 2CFE 39.

Figure 10: Gel electrophoresis of a helicase reaction using 2CFE 21 and 39 and radiolabeled synthetic Holliday Junction template, as described in Example 11, *infra*. Lane 1 contains the synthetic Holliday Junction template; lane 2 contains the synthetic duplex; lane 3 contains a single-stranded template; lane 4 contains the helicase reaction using 2CFE 39; lane 5 contains the helicase reaction using 2CFE 21; lanes 6-8 contain the helicase reaction using 2CFE 39 and 21 at varying concentrations (e.g., 1, 2, and 3  $\mu$ M each); and lane 9 contains the helicase reaction using 2  $\mu$ M each 2CFE 39 and 21 in the presence of ethidium bromide.

20

Figure 11: A graph depicting the results of the helicase reaction which were monitored by measuring the unquenching of the Holliday Junction templates with time, as described in Example 11, *infra*.

25

Figure 12: Capillary electrophoresis results of 2CFE 8 with and without ssDNA, as described in Example 12, *infra*. A) Electropherogram of 2CFE 8 alone. B) Electropherogram of 2CFE 8 in the presence of a 32-nucleotide single-stranded oligomer.

Figure 13: Gel mobility shift assay of 2CFE 8, and 2CFE 8 in the presence of a single-stranded 32-mer, as described in Example 12, *infra*. A) An ethidium bromide-stained,

30

native, polyacrylamide gel containing 2CFE 8, and 2CFE 8 in the presence of a 32-mer. B) The same native, polyacrylamide gel stained with Coomassie.

Figure 14: The N-acetyl glucosamine pathway putatively mediated by 2CFE 3 and 2CFE 86, as described in Example 13, *infra*.

Figure 15: Capillary electrophoresis results of 2CFE 3 with and without putative substrates, as described in Example 13, *infra*. A) Electropherogram of 2CFE 3 with and without glucosamine-1-phosphate. B) Electropherogram of 2CFE 3 with and without D-glucose-1-phosphate. C) Electropherogram of 2CFE 3 alone, 2CFE 3 and glucose-1-phosphate, and 2CFE 3 and glucose-6-phosphate. D) Electropherogram of 2CFE 3 alone or in the presence of glucosamine-1-phosphate, glucosamine-6-phosphate, D-glucose, D(+) galactose, and  $\alpha$ -D-glucose-1-phosphate.

Figure 16: Capillary electrophoresis results of FITC-derivitized 2CFE 3 polypeptide with and without D-glucosamine-6-phosphate (substrate) to produce the product D-glucosamine-1-phosphate, using laser-induced fluorescence, as described in Example 13, *infra*. Electropherogram of D-glucosamine-6-phosphate (putative substrate), 2CFE 3 reacted with D-glucosamine-6-phosphate, and the product glucosamine-1-phosphate.

Figure 17: Gel electrophoresis of 2CFE 86 eluted from an Ni-NTA column, as described in Example 13, *infra*.

Figure 18: HPLC analysis of a coupled reaction including 2CFE 3, 2CFE 86, and D-glucosamine-6-phosphate to produce the product, UDP-N-acetylglucosamine-1-phosphate (UDPAG), as described in Example 13, *infra*.

Figure 19: A fatty acid biosynthesis pathway.

Figure 20: Size exclusion chromatography to determine the molecular weight and oligomeric form of 2CFE 34, as described in Example 14, *infra*. Selected eluted samples were sized by gel electrophoresis.

- 5    Figure 21: Gel electrophoresis of 2CFE 41 eluted from a Ni-NTA column, as described in Example 15, *infra*.

Figure 22: Capillary electrophoresis results of 2CFE 40, 41, and 46, as described in Example 15, *infra*.

10

Figure 23: Depicts a schematic diagram of a ligand which binds 2CFE 34. The ligand is 2-phenyl-N-(3 carboxyl-4-hydroxyphenyl) azabicyclo [4.3.0] nona-2, 8-diene.

- 15    Figure 24: Depicts a schematic diagram of a ligand which binds 2CFE 43. The ligand is N-(3, 5-dinitrobenzyl)-7-trifluoromethyl benza diaza furanolactone.

Figure 25: Depicts a schematic diagram of a ligand which binds 2CFE 43. The ligand is 2-amino (N-para-methylphenyl sulfonamide)-3-phenylpropanoic acid.

- 20    Figure 26: A nucleic acid sequence of 2CFE1 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 27: A nucleic acid sequence of 2CFE2 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 28: A nucleic acid sequence of 2CFE3 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- Figure 29: A nucleic acid sequence of 2CFE4 deposited with the American Type Culture  
30    Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 30: A nucleic acid sequence of 2CFE5 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- 5 Figure 31: A nucleic acid sequence of 2CFE6 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 32: A nucleic acid sequence of 2CFE7 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 33: A nucleic acid sequence of 2CFE8 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- Figure 34: A nucleic acid sequence of 2CFE9 deposited with the American Type Culture  
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Figure 35: A nucleic acid sequence of 2CFE10 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- 20 Figure 36: A nucleic acid sequence of 2CFE11 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 37: A nucleic acid sequence of 2CFE12 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 38: A nucleic acid sequence of 2CFE13 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

- Figure 39: A nucleic acid sequence of 2CFE14 deposited with the American Type Culture  
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Figure 40: A nucleic acid sequence of 2CFE15 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 41: A nucleic acid sequence of 2CFE16 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 42: A nucleic acid sequence of 2CFE17 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 43: A nucleic acid sequence of 2CFE19 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 44: A nucleic acid sequence of 2CFE21 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 45: A nucleic acid sequence of 2CFE24 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 46: A nucleic acid sequence of 2CFE25 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 47: A nucleic acid sequence of 2CFE26 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 48: A nucleic acid sequence of 2CFE27 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 49: A nucleic acid sequence of 2CFE28 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 50: A nucleic acid sequence of 2CFE29 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 51: A nucleic acid sequence of 2CFE30 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 52: A nucleic acid sequence of 2CFE31 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 53: A nucleic acid sequence of 2CFE32 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 54: A nucleic acid sequence of 2CFE33 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 55: A nucleic acid sequence of 2CFE34 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 56: A nucleic acid sequence of 2CFE35 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 57: A nucleic acid sequence of 2CFE36 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 59: A nucleic acid sequence of 2CFE38 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 60: A nucleic acid sequence of 2CFE39 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 62: A nucleic acid sequence of 2CFE41 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 63: A nucleic acid sequence of 2CFE42 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 64: A nucleic acid sequence of 2CFE43 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 65: A nucleic acid sequence of 2CFE44 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 66: A nucleic acid sequence of 2CFE45 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 67: A nucleic acid sequence of 2CFE46 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 69: A nucleic acid sequence of 2CFE48 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 70: A nucleic acid sequence of 2CFE49 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 71: A nucleic acid sequence of 2CFE50 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 72: A nucleic acid sequence of 2CFE51 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 74: A nucleic acid sequence of 2CFE53 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 75: A nucleic acid sequence of 2CFE54 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 76: A nucleic acid sequence of 2CFE55 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 77: A nucleic acid sequence of 2CFE56 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 79: A nucleic acid sequence of 2CFE58 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 80: A nucleic acid sequence of 2CFE59 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 81: A nucleic acid sequence of 2CFE60 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 82: A nucleic acid sequence of 2CFE61 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 83: A nucleic acid sequence of 2CFE62 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 84: A nucleic acid sequence of 2CFE64 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 85: A nucleic acid sequence of 2CFE65 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 86: A nucleic acid sequence of 2CFE66 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 87: A nucleic acid sequence of 2CFE67 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 88: A nucleic acid sequence of 2CFE68 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 89: A nucleic acid sequence of 2CFE69 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 90: A nucleic acid sequence of 2CFE70 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 91: A nucleic acid sequence of 2CFE71 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 92: A nucleic acid sequence of 2CFE72 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 93: A nucleic acid sequence of 2CFE75 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 94: A nucleic acid sequence of 2CFE76 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 95: A nucleic acid sequence of 2CFE78 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 96: A nucleic acid sequence of 2CFE79 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 97: A nucleic acid sequence of 2CFE80 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 98: A nucleic acid sequence of 2CFE81 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 99: A nucleic acid sequence of 2CFE82 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 100: A nucleic acid sequence of 2CFE83 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 101: A nucleic acid sequence of 2CFE84 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 102: A nucleic acid sequence of 2CFE85 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 103: A nucleic acid sequence of 2CFE86 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 104: A nucleic acid sequence of 2CFE87 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 105: A nucleic acid sequence of 2CFE88 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 106: A nucleic acid sequence of 2CFE89 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 107: A nucleic acid sequence of 2CFE90 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 108: A nucleic acid sequence of 2CFE91 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 109: A nucleic acid sequence of 2CFE92 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 110: A nucleic acid sequence of 2CFE94 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 111: A nucleic acid sequence of 2CFE95 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 112: A nucleic acid sequence of 2CFE96 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 113: A nucleic acid sequence of 2CFE97 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 114: A nucleic acid sequence of 2CFE99 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 115: A nucleic acid sequence of 2CFE101 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

20 Figure 116: A nucleic acid sequence of 2CFE102 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 117: A nucleic acid sequence of 2CFE103 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 118: A nucleic acid sequence of 2CFE104 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 119: A nucleic acid sequence of 2CFE105 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 120: A nucleic acid sequence of 2CFE106 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

5 Figure 121: A nucleic acid sequence of 2CFE107 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 122: A nucleic acid sequence of 2CFE108 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

10 Figure 123: A nucleic acid sequence of 2CFE109 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 124: A nucleic acid sequence of 2CFE111 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 125: A nucleic acid sequence of 2CFE112 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 126: A nucleic acid sequence of 2CFE113 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

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Figure 127: A nucleic acid sequence of 2CFE114 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

25 Figure 128: A nucleic acid sequence of 2CFE115 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 129: A nucleic acid sequence of 2CFE116 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

30

Figure 130: A nucleic acid sequence of 2CFE117 deposited with the American Type Culture Collection as ATCC designation \_\_\_\_\_ on December 20, 2000.

Figure 131: Schematic structures of alkylolids which are ligands, for example, of 2CFE42.

5

## **DETAILED DESCRIPTION OF THE INVENTION**

### **Definitions**

10 All scientific and technical terms used in this application have meanings commonly used in the art unless otherwise specified. As used in this application, the following words or phrases have the meanings specified.

As used herein, a *ceg* nucleic acid molecule is said to be "isolated" when the nucleic acid  
15 molecule is substantially separated from contaminant nucleic acid molecules that encode polypeptides other than CEGs. Additionally, isolated nucleic acid molecule refers to any RNA or DNA sequence obtained from a natural source, or constructed by recombinant methods, or synthesized. A skilled artisan can readily employ nucleic acid isolation procedures to obtain an isolated nucleic acid molecule having *ceg* sequences.

20

The term "*ceg*" includes all isolated forms of *ceg* nucleotide and CEG amino acid sequences disclosed herein. The *ceg* sequences encode gene products that have essential biological functions in bacterial cells, such as, for example, nucleotide biosynthesis, amino acid biosynthesis, DNA replication, RNA transcription, protein translation, DNA  
25 recombination, DNA repair, biosynthesis of cofactors (e.g., Coenzyme A), biosynthesis of prosthetic groups, cellular processes (e.g., chaperones, cell division, and polypeptide secretion), energy metabolism (e.g., pentose phosphate pathway, glycolysis, gluconeogenesis), fatty acid biosynthesis, cell wall biosynthesis, and/or biosynthesis of purines, pyrimidines, nucleosides, and nucleotides. Accordingly, the gene products of the  
30 *ceg* nucleotide sequences are required for viability of bacterial cells. The term "*ceg*" also includes variants having nucleotide sequence similarity to the disclosed *ceg* sequences,



including sequences isolated from various bacterial genera and species, allelic variants, mutant variants, and *ceg* variants that encode conservative and non-conservative amino acid substitutions. The present invention also provides for all *ceg* sequences generated by recombinant DNA technology, including complementary sequences, *ceg* sequences that  
5 hybridize to the sequences of the invention at high stringency hybridization conditions, fusion genes comprising a *ceg* sequence, and codon usage variants.

The term "essential genes" refers to a nucleotide sequence that encodes a gene product having a function which is required for cell viability. The term "essential protein" refers  
10 to a polypeptide that is encoded by an essential gene and has a function that is required for cell viability. Accordingly, a mutation that disrupts the function of the essential gene or essential proteins results in a loss of viability of cells harboring the mutation.

"Non-essential genes" or "non-essential proteins" refer to genomic information or the  
15 protein(s) or RNAs encoded therefrom which, when disrupted by a mutation, do not result in a loss of viability of cells harboring said mutation under defined laboratory conditions.

As used herein, a nucleotide sequence is said to be "identical" to another reference  
20 sequence when both nucleotide sequences are exactly alike.

As used herein, a nucleotide sequence is said to be "similar" to another reference sequence when a comparison of the two sequences shows that they have a low level of sequence differences. For example, two sequences are considered to be similar to each  
25 other when the percentage of nucleotides that are shared between the two sequences is between about 70 % to 99.99% over the entire length of the two sequences.

As used herein an amino acid sequence is said to be "similar" to another reference sequence when a comparison of the two sequences shows that they have a low level of  
30 sequence differences. For example, two sequences are considered to be similar to each

other when the percentage of amino acids that are shared between the two sequences may be between about 30% to 100% identity over the entire length of the two sequences.

As used herein, an "allele" or "allelic sequence" is an alternative form of the naturally-  
5 occurring *ceg* sequence. Alleles result from a mutation, that changes the nucleotide sequence, and generally produce altered mRNAs or polypeptides whose structure or function may or may not be altered.

"Substantially purified" as used herein means a specific isolated nucleic acid or protein,  
10 or fragment thereof, in which substantially all contaminants (i.e. substances that differ from said specific molecule) have been separated from said nucleic acid or protein.

In a host cell, an "endogenous" sequence as used herein means a nucleic acid sequence that is naturally-occurring and resides within the host genome.

15

In a host cell, an "exogenous" sequence as used herein means an isolated nucleic acid sequence that is introduced into the host cell, using any one of a variety of introduction methods, such as transfection, electroporation, cationic lipid or salt treatment methods.

20 "Knockout mutant" or "knockout mutation" as used herein refers to an *in vitro* engineered disruption of a region of endogenous chromosomal DNA (e.g., disruption of the genome), typically within a protein coding region. A knockout mutation can be generated by inserting an exogenous DNA sequence into the homologous endogenous sequence. A knockout mutation occurring in a protein coding region is expected to disrupt normal  
25 expression of the protein coding region. This usually leads to loss of the function provided by the protein.

In order that the invention herein described may be more fully understood, the following description is set forth.

30

## A) MOLECULES OF THE INVENTION

### 1.) CEG NUCLEIC ACID MOLECULES

- 5 The present invention provides isolated and recombinant *ceg* nucleic acid molecules and fragments thereof, and related molecules, such as sequences complementary to *ceg* sequences or a portion thereof, and those that hybridize to the nucleic acid molecules of the invention.
- 10 The *ceg* polynucleotide sequences, also referred to herein as nucleic acid molecules of the invention, are preferably in isolated form, including DNA, RNA, DNA/RNA hybrids, and related molecules, and fragments thereof. Specifically contemplated are genomic DNA, ribozymes, and antisense molecules, as well as nucleic acid molecules based on an alternative backbone or including alternative bases, whether derived from natural sources or
- 15 synthesized. Embodiments of particular *ceg* polynucleotide and amino acid sequences include, but are not limited to, the sequences described in Tables I and II (e.g., SEQ ID NOS:1-113, 114-226 and SEQ ID NOS: 227-339, 340-452, respectively). The *ceg* polynucleotide and amino acid sequences were designated *cfe* which stands for CEG For Expression.
- 20 Biological samples of the 2CFE nucleic acid molecules (e.g., SEQ ID NOS: 227-331) were deposited on December 20, 2000 with the American Type Culture Collection (ATCC), 10801 University Blvd., Manassas, VA 20110-2209.

TABLE I

| CFE Designation | SEQ. ID NO.<br>(Nucleotide) | SEQ. ID NO.<br>(Polypeptide) | POLARITY |
|-----------------|-----------------------------|------------------------------|----------|
| CFE 1           | 1                           | 114                          | +        |
| CFE 2           | 2                           | 115                          | -        |
| CFE 3           | 3                           | 116                          | -        |
| CFE 4           | 4                           | 117                          | +        |
| CFE 5           | 5                           | 118                          | -        |
| CFE 6           | 6                           | 119                          | +        |

TABLE I

| CFE Designation | SEQ. ID NO.<br>(Nucleotide) | SEQ. ID NO.<br>(Polypeptide) | POLARITY |
|-----------------|-----------------------------|------------------------------|----------|
| CFE 7           | 7                           | 120                          | -        |
| CFE 8           | 8                           | 121                          | +        |
| CFE 9           | 9                           | 122                          | +        |
| CFE 10          | 10                          | 123                          | +        |
| CFE 11          | 11                          | 124                          | +        |
| CFE 12          | 12                          | 125                          | +        |
| CFE 13          | 13                          | 126                          | -        |
| CFE 14          | 14                          | 127                          | +        |
| CFE 15          | 15                          | 128                          | -        |
| CFE 16          | 16                          | 129                          | -        |
| CFE 17          | 17                          | 130                          | -        |
| CFE 19          | 18                          | 131                          | +        |
| CFE 21          | 19                          | 132                          | -        |
| CFE 24          | 20                          | 133                          | -        |
| CFE 25          | 21                          | 134                          | +        |
| CFE 26          | 22                          | 135                          | -        |
| CFE 27          | 23                          | 136                          | +        |
| CFE 28          | 24                          | 137                          | -        |
| CFE 29          | 25                          | 138                          | -        |
| CFE 30          | 26                          | 139                          | -        |
| CFE 31          | 27                          | 140                          | +        |
| CFE 32          | 28                          | 141                          | +        |
| CFE 33          | 29                          | 142                          | -        |
| CFE 34          | 30                          | 143                          | +        |
| CFE 35          | 31                          | 144                          | +        |
| CFE 36          | 32                          | 145                          | +        |
| CFE 37          | 33                          | 146                          | -        |
| CFE 38          | 34                          | 147                          | +        |
| CFE 39          | 35                          | 148                          | -        |
| CFE 40          | 36                          | 149                          | -        |
| CFE 41          | 37                          | 150                          | -        |
| CFE 42          | 38                          | 151                          | -        |
| CFE 43          | 39                          | 152                          | -        |
| CFE 44          | 40                          | 153                          | +        |
| CFE 45          | 41                          | 154                          | -        |
| CFE 46          | 42                          | 155                          | -        |

TABLE I

| CFE Designation | SEQ. ID NO.<br>(Nucleotide) | SEQ. ID NO.<br>(Polypeptide) | POLARITY |
|-----------------|-----------------------------|------------------------------|----------|
| CFE 47          | 43                          | 156                          | -        |
| CFE 48          | 44                          | 157                          |          |
| CFE 49          | 45                          | 158                          | +        |
| CFE 50          | 46                          | 159                          | +        |
| CFE 51          | 47                          | 160                          | +        |
| CFE 52          | 48                          | 161                          | -        |
| CFE 53          | 49                          | 162                          | +        |
| CFE 54          | 50                          | 163                          | +        |
| CFE 55          | 51                          | 164                          | +        |
| CFE 56          | 52                          | 165                          | +        |
| CFE 57          | 53                          | 166                          | +        |
| CFE 58          | 54                          | 167                          | +        |
| CFE 59          | 55                          | 168                          | -        |
| CFE 60          | 56                          | 169                          | +        |
| CFE 61          | 57                          | 170                          | +        |
| CFE 62          | 58                          | 171                          |          |
| CFE 63          | 59                          | 172                          |          |
| CFE 64          | 60                          | 173                          | +        |
| CFE 65          | 61                          | 174                          | +        |
| CFE 66          | 62                          | 175                          | +        |
| CFE 67          | 63                          | 176                          | +        |
| CFE 68          | 64                          | 177                          | -        |
| CFE 69          | 65                          | 178                          | +        |
| CFE 70          | 66                          | 179                          | +        |
| CFE 71          | 67                          | 180                          | -        |
| CFE 72          | 68                          | 181                          | -        |
| CFE 73          | 69                          | 182                          | +        |
| CFE 74          | 70                          | 183                          | -        |
| CFE 75          | 71                          | 184                          | -        |
| CFE 76          | 72                          | 185                          | +        |
| CFE 77          | 73                          | 186                          |          |
| CFE 78          | 74                          | 187                          | +        |
| CFE 79          | 75                          | 188                          | -        |
| CFE 80          | 76                          | 189                          | -        |
| CFE 81          | 77                          | 190                          | +        |
| CFE 82          | 78                          | 191                          |          |

TABLE I

| CFE Designation | SEQ. ID NO.<br>(Nucleotide) | SEQ. ID NO.<br>(Polypeptide) | POLARITY |
|-----------------|-----------------------------|------------------------------|----------|
| CFE 83          | 79                          | 192                          | -        |
| CFE 84          | 80                          | 193                          | -        |
| CFE 85          | 81                          | 194                          | -        |
| CFE 86          | 82                          | 195                          | -        |
| CFE 87          | 83                          | 196                          | -        |
| CFE 88          | 84                          | 197                          | -        |
| CFE 89          | 85                          | 198                          | +        |
| CFE 90          | 86                          | 199                          | +        |
| CFE 91          | 87                          | 200                          | -        |
| CFE 92          | 88                          | 201                          | -        |
| CFE 93          | 89                          | 202                          | +        |
| CFE 94          | 90                          | 203                          | +        |
| CFE 95          | 91                          | 204                          | +        |
| CFE 96          | 92                          | 205                          | +        |
| CFE 97          | 93                          | 206                          | -        |
| CFE 98          | 94                          | 207                          |          |
| CFE 99          | 95                          | 208                          | +        |
| CFE 100         | 96                          | 209                          |          |
| CFE 101         | 97                          | 210                          | -        |
| CFE 102         | 98                          | 211                          | +        |
| CFE 103         | 99                          | 212                          | -        |
| CFE 104         | 100                         | 213                          | +        |
| CFE 105         | 101                         | 214                          | -        |
| CFE 106         | 102                         | 215                          | -        |
| CFE 107         | 103                         | 216                          | -        |
| CFE 108         | 104                         | 217                          | +        |
| CFE 109         | 105                         | 218                          | -        |
| CFE110          | 106                         | 219                          | -        |
| CFE 111         | 107                         | 220                          | -        |
| CFE 112         | 108                         | 221                          | -        |
| CFE 113         | 109                         | 222                          | -        |
| CFE 114         | 110                         | 223                          | -        |
| CFE 115         | 111                         | 224                          | -        |
| CFE 116         | 112                         | 225                          | -        |
| CFE 117         | 113                         | 226                          | -        |

TABLE II

| CFE Designation | SEQ. ID NO.<br>(Nucleotide) | SEQ. ID NO.<br>(Polypeptide) | FIGURE |
|-----------------|-----------------------------|------------------------------|--------|
| 2CFE 1          |                             |                              | 26     |
| 2CFE 2          |                             |                              | 27     |
| 2CFE 3          |                             |                              | 28     |
| 2CFE 4          |                             |                              | 29     |
| 2CFE 5          |                             |                              | 30     |
| 2CFE 6          |                             |                              | 31     |
| 2CFE 7          |                             |                              | 32     |
| 2CFE 8          |                             |                              | 33     |
| 2CFE 9          |                             |                              | 34     |
| 2CFE 10         |                             |                              | 35     |
| 2CFE 11         |                             |                              | 36     |
| 2CFE 12         |                             |                              | 37     |
| 2CFE 13         |                             |                              | 38     |
| 2CFE 14         |                             |                              | 39     |
| 2CFE 15         |                             |                              | 40     |
| 2CFE 16         |                             |                              | 41     |
| 2CFE 17         |                             |                              | 42     |
| 2CFE 19         |                             |                              | 43     |
| 2CFE 21         |                             |                              | 44     |
| 2CFE 24         |                             |                              | 45     |
| 2CFE 25         |                             |                              | 46     |
| 2CFE 26         |                             |                              | 47     |
| 2CFE 27         |                             |                              | 48     |
| 2CFE 28         |                             |                              | 49     |
| 2CFE 29         |                             |                              | 50     |
| 2CFE 30         |                             |                              | 51     |
| 2CFE 31         |                             |                              | 52     |
| 2CFE 32         |                             |                              | 53     |
| 2CFE 33         |                             |                              | 54     |
| 2CFE 34         |                             |                              | 55     |
| 2CFE 35         |                             |                              | 56     |
| 2CFE 36         |                             |                              | 57     |
| 2CFE 37         |                             |                              | 58     |
| 2CFE 38         |                             |                              | 59     |
| 2CFE 39         |                             |                              | 60     |

| CFE Designation | SEQ. ID NO.<br>(Nucleotide) | SEQ. ID NO.<br>(Polypeptide) | FIGURE |
|-----------------|-----------------------------|------------------------------|--------|
| 2CFE 40         |                             |                              | 61     |
| 2CFE 41         |                             |                              | 62     |
| 2CFE 42         |                             |                              | 63     |
| 2CFE 43         |                             |                              | 64     |
| 2CFE 44         |                             |                              | 65     |
| 2CFE 45         |                             |                              | 66     |
| 2CFE 46         |                             |                              | 67     |
| 2CFE 47         |                             |                              | 68     |
| 2CFE 48         |                             |                              | 69     |
| 2CFE 49         |                             |                              | 70     |
| 2CFE 50         |                             |                              | 71     |
| 2CFE 51         |                             |                              | 72     |
| 2CFE 52         |                             |                              | 73     |
| 2CFE 53         |                             |                              | 74     |
| 2CFE 54         |                             |                              | 75     |
| 2CFE 55         |                             |                              | 76     |
| 2CFE 56         |                             |                              | 77     |
| 2CFE 57         |                             |                              | 78     |
| 2CFE 58         |                             |                              | 79     |
| 2CFE 59         |                             |                              | 80     |
| 2CFE 60         |                             |                              | 81     |
| 2CFE 61         |                             |                              | 82     |
| 2CFE 62         |                             |                              | 83     |
| 2CFE 64         |                             |                              | 84     |
| 2CFE 65         |                             |                              | 85     |
| 2CFE 66         |                             |                              | 86     |
| 2CFE 67         |                             |                              | 87     |
| 2CFE 68         |                             |                              | 88     |
| 2CFE 69         |                             |                              | 89     |
| 2CFE 70         |                             |                              | 90     |
| 2CFE 71         |                             |                              | 91     |
| 2CFE 72         |                             |                              | 92     |
| 2CFE 75         |                             |                              | 93     |
| 2CFE 76         |                             |                              | 94     |
| 2CFE 78         |                             |                              | 95     |
| 2CFE 79         |                             |                              | 96     |
| 2CFE 80         |                             |                              | 97     |



| CFE Designation | SEQ. ID NO.<br>(Nucleotide) | SEQ. ID NO.<br>(Polypeptide) | FIGURE |
|-----------------|-----------------------------|------------------------------|--------|
| 2CFE 81         |                             |                              | 98     |
| 2CFE 82         |                             |                              | 99     |
| 2CFE 83         |                             |                              | 100    |
| 2CFE 84         |                             |                              | 101    |
| 2CFE 85         |                             |                              | 102    |
| 2CFE 86         |                             |                              | 103    |
| 2CFE 87         |                             |                              | 104    |
| 2CFE 88         |                             |                              | 105    |
| 2CFE 89         |                             |                              | 106    |
| 2CFE 90         |                             |                              | 107    |
| 2CFE 91         |                             |                              | 108    |
| 2CFE 92         |                             |                              | 109    |
| 2CFE 94         |                             |                              | 110    |
| 2CFE 95         |                             |                              | 111    |
| 2CFE 96         |                             |                              | 112    |
| 2CFE 97         |                             |                              | 113    |
| 2CFE 99         |                             |                              | 114    |
| 2CFE 101        |                             |                              | 115    |
| 2CFE 102        |                             |                              | 116    |
| 2CFE 103        |                             |                              | 117    |
| 2CFE 104        |                             |                              | 118    |
| 2CFE 105        |                             |                              | 119    |
| 2CFE 106        |                             |                              | 120    |
| 2CFE 107        |                             |                              | 121    |
| 2CFE 108        |                             |                              | 122    |
| 2CFE 109        |                             |                              | 123    |
| 2CFE 111        |                             |                              | 124    |
| 2CFE 112        |                             |                              | 125    |
| 2CFE 113        |                             |                              | 126    |
| 2CFE 114        |                             |                              | 127    |
| 2CFE 115        |                             |                              | 128    |
| 2CFE 116        |                             |                              | 129    |
| 2CFE 117        |                             |                              | 130    |

### a) Variant *ceg* Nucleotide Sequences

The present invention also provides nucleic acid molecules having a nucleotide sequence  
5 substantially identical or similar to the *ceg* sequences (SEQ ID NOS: 1-113, 227-331)  
disclosed herein.

The present invention provides nucleotide sequences which are similar to SEQ ID  
NOS:1-113 and/or SEQ ID NOS:227-331. The present invention provides nucleotide  
10 sequences which vary from SEQ ID NOS:1-113 or 227-331 by a range of about 1% to  
about 70%.

The present invention encompasses variations in polynucleotide sequences resulting from  
mutations and/or from transfer of genetic material from one cell to another (e.g.,  
15 horizontal gene transfer or horizontal gene exchange).

The present invention also provides for variants of the polynucleotide *ceg* sequences  
disclosed herein, including variants isolated from naturally-occurring sources, those  
generated by recombinant DNA technology or other in vitro synthesis methodologies  
20 (e.g., PCR). The variant polynucleotide sequences of the invention encode polypeptides  
that exhibit the biological activity of naturally-occurring CEG polypeptides, such as  
activity required for bacterial cell viability.

In general, for example, a variant of *ceg* polynucleotide sequences may encode a  
25 polypeptide that differs by one or more amino acid substitutions. The variant may have  
conservative changes, wherein a substituted amino acid has similar structural or chemical  
properties, eg, replacement of leucine with isoleucine.

A polynucleotide sequence can encode conservative amino acid substitutions without  
30 altering either the conformation or the function of the polypeptide. Such changes include  
substituting any of isoleucine (I), valine (V), and leucine (L) for any other of these

hydrophobic amino acids; aspartic acid (D) for glutamic acid (E) and vice versa; glutamine (Q) for asparagine (N) and vice versa; and serine (S) for threonine (T) and vice versa. Other substitutions can also be considered conservative, depending on the environment of the particular amino acid and its role in the three-dimensional structure of the protein. For example, glycine (G) and alanine (A) can frequently be interchangeable, as can alanine (A) and valine (V). Methionine (M), which is relatively hydrophobic, can frequently be interchanged with leucine and isoleucine, and sometimes with valine. Lysine (K) and arginine (R) are frequently interchangeable in locations in which the significant feature of the amino acid residue is its charge and the differing pK's of these two amino acid residues are not significant. Still other changes can be considered "conservative" in particular environments.

A variant may also have nonconservative changes, eg, replacement of a glycine with a tryptophan. Other variations may also include amino acid deletions or insertions, or both. Guidance in determining which and how many amino acid residues may be substituted, inserted or deleted without abolishing biological or immunological activity may be found using computer programs well known in the art, for example, DNASTAR software.

Another type of *ceg* sequence variant includes naturally-occurring allelic variants of *ceg* which share significant similarity (e.g., between about 30- 99%) to the disclosed CEG polypeptide sequence. Allelic variants of the *ceg* sequences can encode conservative or non-conservative amino acid substitutions of the CEG polypeptide sequence herein described.

An example of allelic variants of *ceg* are mutant alleles of *ceg* polynucleotide sequences that encode a polypeptide having one or more changes in the polypeptide sequence, such as amino acid substitutions, deletions, insertions, frame shifts, or truncations. The mutant alleles of *ceg* may or may not encode a CEG polypeptide having the same biological functions as wild-type CEG proteins.

Variations in the bacterial genomic sequences can also arise from transfer of genetic material to another bacterial cell. The transfer of gene sequences can occur intraspecies or interspecies. Gene transfer can occur between bacterial cells which are members of the same or different populations. A population includes, but is not limited to, a serotype isolate, a clinical isolate, a naturally-occurring isolate, a strain, and a species. The transfer of genetic material can occur between cells within a population; for example transfer between serotype A to serotype A, or between *S. pneumoniae* and *S. pneumoniae*. The transfer of genetic material can occur between cells of different populations; for example, between serotype A to serotype B or *S. pneumoniae* and *S. mutans*.

Gene transfer can give rise to mutant or polymorphic variant genes sequences. In rare cases, gene transfer introduces new gene sequences that confer a new phenotype, such as antibiotic resistance. The transfer of genetic material includes transfer of large regions of genomic sequences which include partial gene sequences, whole single gene sequences, or multiple gene sequences. This mode of transfer can give rise to replacement of native whole gene sequences or introduction of new sequences in the recipient cell. This mode of transfer gives rise to mosaic gene sequences in the recipient cell.

The variation of genomic sequences resulting from gene transfer can be examined using molecular techniques, including: multilocus enzyme electrophoresis (Selander, R. K., et al., 1986 *Appl. Environ. Microbiol.* 51:837-884); and restriction endonuclease cleavage electrophoretic profiling (Coffey, T. J., et al., 1991 *Mol. Microbio.* 5:2255-2260); pulse-field gel electrophoresis fingerprinting (Bygraves, J. A. and Maiden, M. C. J. 1992 *J. Gen. Microbiol.* 138:523-531); and ribotyping (Stull, T. L., et al., 1988 *J. Infect. Dis.* 157:280-286). The degree of variation can vary greatly, and ranges from little or no variation as exemplified by gene sequences of *E. coli* (Caugant, d. A., et al., 1981 *Genetics* 98:467-490; Whittam, T. S., et al., 1983 *Mol. Biol. Evol.* 1:67-83; Souza, V., et al., 1992 *Proc. Natl. Acad. Sci. USA* 89:8389-8393) and *Salmonella* (Selander, R. K., et al., 1990 *Infect. Immun.* 58:2262-2275; Selander, R.K. and Smith, N. H. 1990 *Rev. Med. Microbiol.* 1:219-228; Smith, J. M., et al., 1993 *Proc. Natl. Acad. Sci. USA* 90:4384-

4388), to extensive gene transfer in *Neisseria gonorrhoeae* (Smith, J. M., et al., 1993 *Proc. Natl. Acad. Sci. USA* 90:4384-4388).

Gene transfer can be examined between various isolates of a particular microbial species  
5 which are antibiotic-sensitive or antibiotic-resistant (Coffey, T. J., et al., 1991 *Molec. Microbiol.* 5:2255-2260). Molecular biology techniques can be utilized to study the degree of transfer between populations, such as, for example, the degree of gene transfer between serotypes, isolates, strains, or species. The degree of transfer can be examined by comparing, for example, the penicillin binding proteins and numerous different loci  
10 which encode metabolic enzymes or capsular biosynthesis enzymes.

For example, intra-species, inter-serotype, gene transfer is possible (Coffey, T. J., et al., 1991 *supra*). Additionally, intraspecies gene transfer in *S. pneumoniae* (Coffey, T. J., et al., 1998 *Mol. Microbiol.* 27:73-83), *Vibrio cholerae* (Bik, E. M., et al., 1995 *EMBO J.*  
15 14:209-216), and *Haemophilus influenzae* (Kroll, J. S. and Moxon, E. R. 1990 *J. Bacteriol.* 172: 1374-1379) are possible.

Interspecies gene transfer is also possible (Dowson, C. G., et al., 1989 *Proc. Natl. Acad. Sci. USA* 86:8842-8846; Laibl, G., et al., 1991 *Mol. Microbiol.* 5:1993-2002; Bourgoin,  
20 F., et al., 1999 *Gene* 233:151-161).

Variant gene sequences arising from gene transfer can be continually generated in transformable bacteria (e.g., transformation competent), such as *S. pneumoniae*. For example, the worldwide spread of varying degrees of antibiotic resistance has been  
25 documented and reviewed (Dowson, C. G., et al., 1994 *Trends Microbiol.* 2:361-366; Spratt, B. G. in *Bacterial Cell Wall*, eds Ghuyssen J-M. and Hakenbeck, R. 1994 pp. 517-534; and reviewed in Maiden, M. C. J. 1998 *Clinic. Infect. Dis.* 27 (Supplement 1) S12-S20). For example, variant gene sequence arising from gene transfer can be tracked using a marker gene such as the gene which encodes the penicillin binding protein  
30 (Barcus, V. A., et al., 1995 *FEMS Microbiol. Lett.* 126:299-303). At the nucleotide level, gene sequences encoding the penicillin binding proteins in susceptible and resistant

strains differ by about 14% to 23% (Hakenbeck, R. 1995 *Biochem. Pharmacol.* 50:1121-1127; Spratt, B. G. in *Bacterial Cell Wall*, eds Ghuysen J-M. and Hakenbeck, R. 1994 pp. 517-534; Spratt, B. G., et al., 1991 *Neisseria meningitidis* and *Streptococcus pneumoniae* eds. Camisi, J., et al., pp. 73-83; Coffey, T. J., et al., 1995 *Micro. Drug Resist.* 1:29-34).

5

The *ceg* nucleotide sequences can be isolated from various species of *Streptococcus* including *Streptococcus pneumoniae*. Additionally, the *ceg* sequences can be isolated from other Streptococcal species, including *S. mutans*, *S. pyogenes*, and *S. thermophila*. The *ceg* polynucleotide sequences can also be isolated from strains of other bacterial genera including, but not limited to, *Streptococcus*, *Escherichia*, *Bacillus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Haemophilus*.

The present invention additionally provides isolated codon-usage variants that differ from the disclosed *ceg* nucleotide sequences, yet do not alter the predicted CEG polypeptide sequence or function. The codon-usage variants may be generated by recombinant DNA technology. Codons may be selected to optimize the level of production of the *ceg* transcript or CEG polypeptide in a particular prokaryotic or eukaryotic expression host, in accordance with the frequency of codon utilized by the host cell. Alternative reasons for altering the nucleotide sequence encoding a CEG polypeptide include the production of RNA transcripts having more desirable properties, such as an extended half-life or increased stability. A multitude of variant *ceg* nucleotide sequences that encode the respective CEG polypeptide may be isolated, as a result of the degeneracy of the genetic code. Accordingly, the present invention contemplates selecting every possible triplet codon to generate every possible combination of nucleotide sequences that encode the disclosed CEG polypeptides. This particular embodiment provides isolated nucleotide sequences that vary from the sequences as described in SEQ ID NOs.: 1-113 or 227-331, such that each variant nucleotide sequence encodes a polypeptide having sequence identity with the amino acid sequences, as described in SEQ ID NOs.: 114-226 or 332-436, respectively.

30

### b) Complementary Sequences

The present invention includes polynucleotide sequences that are complementary to the sequences disclosed herein. The term "complementary" as used herein refers to the capacity of purine and/or pyrimidine nucleotides to associate through hydrogen bonding to form double stranded nucleic acid molecules. The following base pairs are related by complementarity: guanine and cytosine; adenine and thymine; and adenine and uracil. Complementary applies to all base pairs comprising at least two single-stranded nucleic acid molecules.

### c) Sequences Capable of Hybridizing

Another embodiment provides nucleic acid molecules that will hybridize to *ceg* sequences under hybridization conditions. It is readily apparent to one skilled in the art that the stringency of the hybridization condition selected will depend upon the characteristics of the nucleic acid molecule to be hybridized, such as, the length, the degree of complementarity (e.g., exact or non-exact complementarity), the percent A/T content, and the objective of the hybridization experiment.

The hybridization procedure may be performed in low stringency hybridization conditions. Low stringency hybridization conditions will permit hybridization between two nucleic acid molecules that differ from exact complementarity by about 25% to 70%. Hybridization under standard high stringency conditions will occur between two complementary nucleic acid molecules (e.g., 100% exact complementarity) or two complementary nucleic acid molecules that differ from exact complementarity by about 1% to about 70%.

The high stringency hybridization conditions that disfavor non-homologous base pairing are well known in the art. Typically, high stringency hybridization conditions, includes but is not limited to, hybridizing at 50 °C to 65 °C in 5X SSPE, and washing at 50 °C to

65 °C in 0.5X SSPE. Typically, low stringency conditions, includes but is not limited to, hybridizing at 35 °C to 37 °C in 5X SSPE and 40% to 45% formamide and washing at 42 °C in 1-2X SSPE. The conditions and formulas for high stringency hybridization methods are well known in the art and can be readily obtained in *Molecular Cloning; A Laboratory Manual* (2<sup>nd</sup> edition, Sambrook, Fritsch, and Maniatis 1989, Cold Spring Harbor Press) or in *Short Protocols in Molecular Biology* (Ausubel, F. M., et al., 1989, John Wiley & Sons).

#### d) Fragments of *ceg* Sequences

10

The invention further provides nucleic acid molecules having fragments of the *ceg* sequences, such as a portion of the *ceg* sequence (e.g., SEQ ID NOS:1-113, 227-331) disclosed herein. The size of the fragment will be determined by its intended use. For example, the length of the fragment to be used as a nucleic acid probe or PCR primer is  
15 chosen to obtain a relatively small number of false positives during probing or priming. Alternatively, a fragment of the *ceg* sequence may be used to construct a recombinant fusion gene having a *ceg* sequence fused to a non-*ceg* sequence.

The nucleic acid molecules, fragments thereof, and probes and primers of the present  
20 invention are useful for a variety of molecular biology techniques including, for example, hybridization screens of libraries, or detection and quantification of mRNA transcripts as a means for analysis of gene transcription and/or expression. Preferably, the probes and primers are DNA. A probe or primer length of at least 15 base pairs is suggested by theoretical and practical considerations (Wallace, B. and Miyada, G. 1987  
25 "Oligonucleotide Probes for the Screening of Recombinant DNA Libraries" in: *Methods in Enzymology*, 152:432-442, Academic Press). Other lengths of fragments, probes, or primers are possible and routine to determine.

The probes and primers of this invention can be prepared by methods well known to  
30 those skilled in the art (Sambrook, et al. *supra*). In a preferred embodiment the probes



and primers are synthesized by chemical synthesis methods (ed: Gait, M. J. 1984 *Oligonucleotide Synthesis*, IRL Press, Oxford, England).

One embodiment of the present invention provides nucleic acid primers that are  
5 complementary to *ceg* sequences, which allow the specific amplification of nucleic acid molecules of the invention or of any specific parts thereof. Another embodiment provides nucleic acid probes that are complementary for selectively or specifically hybridizing to the *ceg* sequences or to any part thereof.

#### 10 e) Derivative Nucleic Acid Molecules

The nucleic acid molecules of the invention include peptide nucleic acids (PNAs), or derivative molecules such as phosphorothioate, phosphotriester, phosphoramidate, and methylphosphonate, that specifically bind to single-stranded DNA or RNA in a base pair-  
15 dependent manner (Zamecnik, P. C., et al., 1978 *Proc. Natl. Acad. Sci.* 75:280284; Goodchild, P. C., et al., 1986 *Proc. Natl. Acad. Sci.* 83:4143-4146).

PNA molecules comprise a nucleic acid oligomer to which an amino acid residue, such as lysine, and an amino group have been added. These small molecules, also designated  
20 anti-gene agents, stop transcript elongation by binding to their complementary (template) strand of nucleic acid (Nielsen, P. E., et al., 1993 *Anticancer Drug Des* 8:53-63). For example, reviews of methods for synthesis of DNA, RNA, and their analogues can be found in: *Oligonucleotides and Analogues*, eds. F. Eckstein, 1991, IRL Press, New York; *Oligonucleotide Synthesis*, ed. M. J. Gait, 1984, IRL Press, Oxford, England.  
25 Additionally, methods for antisense RNA technology are described in U. S. patents 5,194,428 and 5,110,802. A skilled artisan can readily obtain these classes of nucleic acid molecules using the herein described *ceg* polynucleotide sequences, see for example *Innovative and Perspectives in Solid Phase Synthesis* (1992) Egholm, et al. pp 325-328 or U. S. Patent No. 5,539,082.

30

### f) RNA Molecules

5 The present invention provides RNA molecules that encode the predicted *ceg* gene products. In particular, the RNA molecules of the invention may be isolated full-length or partial mRNA molecules or RNA oligomers that encode CEG gene products. The RNA molecules of the invention include the nucleotide sequences encoding all or portions of CEGs.

10 The RNA molecules of the invention also include antisense RNA molecules, peptide nucleic acids (PNAs), or non-nucleic acid molecules such as phosphorothioate derivatives, that specifically bind to the sense strand of DNA or RNA in a base pair-dependent manner. A skilled artisan can readily obtain these classes of nucleic acid molecules using the herein described *ceg* sequences.

15

### g) Labeled Nucleic Acid Molecules

The nucleic acid molecules having *ceg* sequences can be labeled with a detectable marker. Examples of a detectable marker include, but are not limited to, a radioisotope, a  
20 fluorescent compound, a bioluminescent compound, a chemiluminescent compound, a metal chelator or an enzyme. Technologies for generating labeled DNA and RNA probes are well known in the art (See e.g. Sambrook et al., *supra*).

## 2.) RECOMBINANT NUCLEIC ACID MOLECULES

25

Also provided are recombinant nucleic acid molecules, such as recombinant DNA molecules (rDNAs) that comprise *ceg* sequences or fragments thereof. As used herein, a recombinant DNA molecule is a DNA molecule that has been subjected to molecular manipulation *in vitro*. Methods for generating rDNA molecules are well known in the art, for example, see Sambrook  
30 et al., *Molecular Cloning* (1989), *supra*.

### a) Vectors

The nucleic acid molecules of the invention may be recombinant molecules each comprising the sequence, or portions thereof, of a *ceg* sequence linked to a non-*ceg* sequence. For example, the *ceg* sequence may be fused operatively to a vector to generate a recombinant molecule. The term vector includes, but is not limited to, plasmids, cosmids, and phagemids. A preferred vector includes an autonomously replicating vector comprising a replicon that directs the replication of the rDNA within the appropriate host cell. The preferred vectors can also include an expression control element, such as a promoter sequence, which enables transcription of the inserted *ceg* sequences and can be used for regulating the expression (e.g., transcription and/or translation) of an operably linked *ceg* sequence in an appropriate host cell such as *Escherichia coli*. Expression control elements are known in the art and include, but are not limited to, inducible promoters, constitutive promoters, secretion signals, enhancers, transcription terminators, and other transcriptional regulatory elements. Other expression control elements that are involved in translation are known in the art, and include the Shine-Dalgarno sequence, and initiation and termination codons. The preferred vector also includes at least one selectable marker gene that encodes a gene product that confers drug resistance such as resistance to ampicillin or tetracycline. The vector also comprises multiple endonuclease restriction sites that enable convenient insertion of exogenous DNA sequences.

The preferred vectors for generating *ceg* transcripts and/or the encoded CEG polypeptides are expression vectors which are compatible with prokaryotic host cells. Prokaryotic cell expression vectors are well known in the art and are available from several commercial sources. For example, a pET vectors (e.g., pET-21, Novagen Corp.) may be used to express CEG polypeptides in bacterial host cells.

### b) Recombinant Vectors for Integration

The present invention provides recombinant vectors that may be used to integrate  
5 exogenously provided sequences into the genome of a host cell. The recombinant  
integration vectors of the present invention include a gene that encodes a selectable  
marker and *ceg* sequences; or fragments thereof. The integration vectors are used to  
integrate the *ceg* sequence into a target gene sequence that resides within the bacterial  
10 host genome (e.g., endogenous sequence), thereby disrupting the function of the target  
gene sequence within the bacterial cells. These integration vectors may be used in a gene  
disruption assay to screen candidate *ceg* nucleotide sequences, in order to identify the  
candidate sequences that encode a gene product that is required for bacterial cell viability.

Accordingly, these recombinant integration vectors include candidate *ceg* sequences that  
15 will be screened to determine if the candidate *ceg* sequences encode a gene product that  
is required for cell viability. The candidate *ceg* sequence that is included as part of the  
recombinant integration vector is the "exogenous" *ceg* sequence that is employed as the  
"disrupting" sequence in a gene disruption assay. The *ceg* sequence that resides within  
the host genome is the "endogenous" or "target" *ceg* sequence.

20 The integration event rarely occurs, for example, by non-homologous recombination in  
which a recombinant vector, that includes the exogenous *ceg* sequence, inserts the  
exogenous *ceg* sequence into a random location within the host genome. In a more  
preferred embodiment, the integration event inserts the exogenous *ceg* sequence into a  
25 specific target site within the host genome. The targeted integration event can involve  
homologous recombination in which the integration vector, that includes the exogenous  
*ceg* sequence, inserts the exogenous *ceg* sequence into its homologous target *ceg*  
sequence that resides within the host's genome (e.g., the endogenous *ceg* sequence)  
(Figure 1). Further, the exogenous *ceg* sequence can be used as a disrupting sequence  
30 whereby the homologous recombination event integrates the exogenous *ceg* sequence  
into the endogenous target *ceg* sequence resulting in disruption of the function of the

endogenous *ceg* sequence. For example, disrupting the function of the endogenous *ceg* sequence may result in the loss of bacterial cell viability.

5 An example of a recombinant vector that can be used as an integration vector in *S. pneumoniae* is the pEVP-3 vector (Jean-Pierre Claverys, et al. 1995 *Gene* 164: 123-128). The pEVP-3 vector integrates an exogenous sequence by homologous recombination involving a Campbell-type event (S. Adhya and A. Campbell 1970 *J. Mol. Biol.* 50:481-490). The pEVP-3 vector includes a replicon that functions only in gram-negative bacteria, such as *E. coli*. Therefore, the pEVP-3 vector cannot replicate in *S.*  
10 *pneumoniae*. This vector also contains multiple cloning sites, and confers resistance to chloramphenicol in both a gram-negative and gram-positive bacteria, such as *S. pneumoniae*.

### c) Fusion Gene Sequences

15 A fusion *ceg* gene is another example of a recombinant molecule of the invention. A fusion gene includes a *ceg* sequence operatively fused (e.g., linked) to a non-*ceg* sequence such as, for example, a tag sequence to facilitate isolation and/or purification of the expressed CEG gene product (Kroll, D.J., et al., 1993 *DNA Cell Biol* 12:441-53).

20 Alternatively, a recombinant fusion molecule has a *ceg* sequence of the invention fused to a *ceg* sequence isolated from a different microbial source. For example, the disclosed *ceg* sequences isolated from *S. pneumoniae* can be fused to a *ceg* sequence isolated from a different bacterial species.

25

### 3.) CEG PROTEINS AND POLYPEPTIDE MOLECULES

The invention additionally provides CEG proteins and peptide fragments thereof that are isolated or substantially purified. Embodiments of particular CEG amino acid sequences  
30 are disclosed in Tables I and II (SEQ ID NOS:114-226 and SEQ ID NOS:332-436, respectively).

The present invention also includes polypeptides having sequence variations from the predicted CEG polypeptide sequences disclosed herein, including mutant variants, conservative substitution variants, and similar CEG polypeptides from other prokaryotic organisms. For convenience, such proteins are referred to herein as "CEG proteins",  
5 "CEG polypeptides", or "proteins of the invention".

As used herein, CEG protein refers to a polypeptide having amino acid sequence identity or similarity to any one of the predicted amino acid sequences, as provided in SEQ ID NO.:  
10 114-226 or 332-436. The variant CEG polypeptides can be allelic forms of CEG, such as mutant forms of CEG polypeptides. The present invention also provides conservative substitution-mutants of the CEG proteins that maintain functional activity of wild-type CEG (e.g., the CEG polypeptide is required for bacterial cell viability).

15 The CEG protein may be isolated from any source whether natural, synthetic, semi-synthetic, or recombinant. As used herein, "natural" refers to a polypeptide which is found in nature. Accordingly, the CEG proteins may be isolated from a prokaryotic organism, such as a bacterial strain including, but not limited to, *Streptococcus*, *Escherichia*, *Bacillus*, *Pseudomonas*, *Yersinia*, *Salmonella*, and *Streptomyces*. The CEG  
20 proteins of the invention, and fragments thereof, can also be generated by recombinant methods or chemical synthesis methods.

The CEG polypeptides of the invention are essential for the viability of a bacterial cell. Further, the CEG polypeptides can exhibit at least any one of the following functions: a  
25 pantothenate kinase, a Holliday Junction branch migration protein, a single stranded DNA binding protein, a phosphoglucosamine mutase, an acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase, a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP binding protein, or a 4-aminoimidazole carboxylase. Putative  
30 functions can include, but are not limited to, sugar transferase, teichoic acid biosynthesis, ribosome recycling factor, response regulator, nicotinate phosphoribosyltransferase,

nitropropane dioxygenase, (3R)-hydroxymyristol acyl carrier protein dehydrase, sugar dehydrogenase, murein biosynthesis, cobalimin biosynthesis, ABC transporter, tRNA modification enzyme, arylsulfatase, 16S processing enzyme, tRNA methyl transferase, elongation factor P, signal recognition particle, protein export, undecaprenol kinase, SRP docking domain, diacyl glycerol kinase, dihydopicillinate reductase, HU-DNA binding protein, thiamine biosynthase, GreA transcription elongation factor, dTDP-L-rhamnose synthase, ATP-binding motif, ribose-5-p-3-epimerase-like activity, GTP pyrophosphokinase, acetyl-CoA carboxylase, O-sialoglycoprotein endopeptidase, glucosamine-fructose-6-phosphate aminotransferase, Strpn adhesion-associated ABC-permease, GTP pyrophosphokinase RelA, IMP dehydrogenase, DNA gyrase subunit B, acetyl-CoA carboxylase subunit AccD, phosphoglycerol kinase, acetyl-CoA carboxylase carbonyl transferase, phosphopantetheine adenylyltransferase, oligopeptide transport permease subunit, translocation protein, perM permease, DNA pol III gamma and tau subunits, DNA pol III delta subunit, signal peptidase I, acetyl-coA carboxylase biotin carboxyl carrier protein, protein chain release factor-1, replicative DNA helicase, topoisomerase, pentapeptide-transferase, elongation factor G, spore coat polysaccharide biosynthesis protein C, protein release factor B, DNA polymerase III alpha subunit, phosphoprotein phosphatase, chaparonin, UDP-N-acetylmuramoylalanyl-D-glutamate-2, 6-diaminopimelate ligase, teichuronic acid biosynthesis, UDP-glucose lipid carrier transferase, transcription termination factor, chromosome segregation factor, amino acid biosynthesis, HMG-CoA reductase, hypoxanthine-guanine phosphoribosyltransferase.

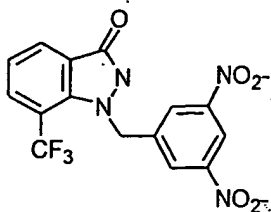
a) **MODULATORS OF CEG POLYPEPTIDES**

The invention provides compounds that modulate (e.g., activate or inhibit) the function of a CEG polypeptide. Such compounds can provide lead-compounds for developing drugs for diagnosing and/or treating conditions associated with bacterial infections. The modulator is a compound that may alter the function of the CEG polypeptide, such as activating or inhibiting the function of a CEG polypeptide. For example, the compound can act as agonist, antagonist, partial agonist, partial antagonist, cytotoxic agents,

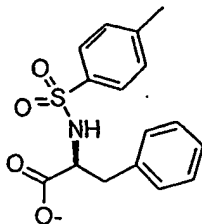
inhibitors of cell proliferation, and cell proliferation-promoting agents. The activity of the compound may be known, unknown or partially known.

Suitable ligands include, but are not limited to, diazalactones, *N*-protected amino acid,  
5 azabicyclodiene, and alkaloids.

An example of a diazalactone is:

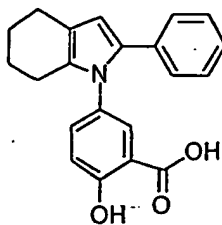


An example of a *N*-protected amino acid is:



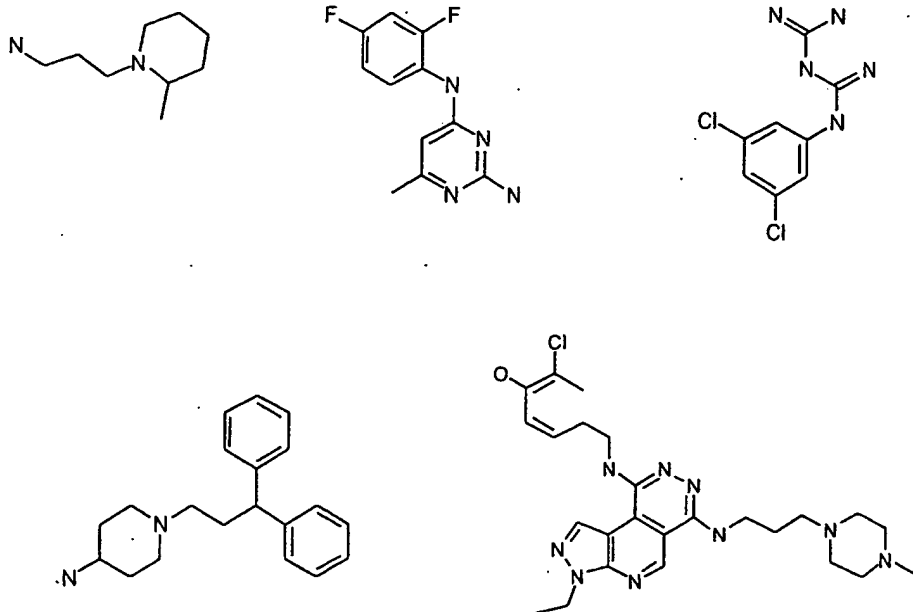
10

An example of an azabicyclodiene is:





Examples of alkaloids are:



## 5 B) METHODS FOR MAKING THE CEG PROTEINS AND POLYPEPTIDES

Recombinant methods are preferred if a high yield is desired. Recombinant methods involve expressing the cloned gene in a suitable host cell. For example, a host cell is introduced with an expression vector having the CEG sequence, then the host cell is

10 cultured under conditions that permit *in vivo* production of the CEG protein. The recombinant vector can integrate the CEG sequence into the host genome. Alternatively, the CEG sequence can be maintained extra-chromosomally, as part of an autonomously replicating vector.

### 15 1. HOST-VECTOR SYSTEMS

The invention further provides a host-vector system comprising the vector, plasmid, phagemid, or cosmid comprising a *ceg* nucleotide sequence, or a fragment thereof, introduced into a suitable host cell. The host-vector system can be used to produce the

CEG polypeptides encoded by the *ceg* nucleotide sequences. The host cell can be prokaryotic or eukaryotic. Examples of suitable prokaryotic host cells include bacteria strains from genera such as *Escherichia*, *Bacillus*, *Pseudomonas*, *Streptococcus*, and *Streptomyces*. Examples of suitable eukaryotic host cells include a yeast cell, a plant cell,  
5 or an animal cell, such as a mammalian cell. A preferred embodiment provides a host-vector system comprising the pET21 vector having a *ceg* sequence introduced into an *E. coli*  $\lambda$ DE3 lysogen which is useful, for example for the production of the CEG protein, herein designated CFE polypeptides and CFE proteins.

- 10 Introduction of the rDNA molecules of the present invention into an appropriate cell host is accomplished by well known methods that typically depend on the type of vector used and host system employed. For example, transformation of prokaryotic host cells by electroporation and salt treatment methods are typically employed, see for example, Cohen et al., 1972 *Proc Acad Sci USA* 69:2110; Maniatis, T., et al., 1989 *Molecular Cloning, A*  
15 *Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY. Transformation of vertebrate cells with vectors containing rDNAs, electroporation, cationic lipid or salt treatment methods are typically employed, see, for example, Graham et al., 1973 *Virol* 52:456; Wigler et al., 1979 *Proc Natl Acad Sci USA* 76:1373-76.
- 20 Successfully transformed cells, i.e., cells that contain a rDNA molecule of the present invention, can be identified by well known techniques. For example, cells resulting from the introduction of a rDNA of the present invention can be selected and cloned to produce single colonies. Cells from those colonies can be harvested, lysed and their DNA content examined for the presence of the rDNA using a method such as that described by Southern,  
25 *J Mol Biol* (1975) 98:503, or Berent et al., *Biotech* (1985) 3:208, or the proteins produced from the cell assayed via a biochemical assay or immunological method.

Procaryotes are generally used as host cells for cloning and producing the products of exogenous DNA sequences. For example, the *Escherichia coli* K12 BL21 ( $\lambda$ DE3)  
30 (Novagen) is particularly useful for expression of foreign proteins. Other strains of *E. coli*, and bacilli such as *Bacillus subtilis*, Enterobacteriaceae such as *Salmonella*

*typhimurium* or *Serratia marcescans*, various *Pseudomonas*, *Streptococcus*, and *Streptomyces* species may also be employed as host cells in cloning and expressing the recombinant proteins of this invention.

- 5 In general terms, the production of recombinant CEG proteins may involve using a host/vector system, or other methods may be used. The host/vector system may employ the following steps.

10 A nucleic acid molecule is obtained that encodes a CEG protein or a fragment thereof, such as any one of the polynucleotides disclosed in SEQ ID NOs.: 1-113 or 227-331. The CEG-encoding nucleic acid molecule is preferably inserted into an expression vector in operable linkage with suitable expression control sequences, to generate an expression vector including the CEG-encoding sequence. The expression vector is introduced into a suitable host, by standard transformation methods, and the resulting transformed host is cultured  
15 under conditions that allow the production of the CEG protein. For example, if expression of the CEG gene is under the control of an inducible promoter, then suitable growth conditions would include the appropriate inducer. The CEG protein (e.g., designated a CFE polypeptide or protein), so produced, is isolated from the growth medium or directly from the cells; recovery and purification of the protein may not be necessary in some  
20 instances where some impurities may be tolerated. A skilled artisan can readily adapt an appropriate host/expression system known in the art for use with CEG-encoding sequences to produce a CEG protein (Cohen, et al., *supra*; Maniatis et al., *supra*).

Host cells harboring the nucleic acids disclosed herein are also provided by the present  
25 invention. A preferred host is *E. coli* strain BL21(λDE3) transfected or transformed with a vector comprising a nucleic acid of the present invention. The invention also provides a host cell capable of expressing the *ceg* sequences described herein. The preferred host cell is any strain of *E. coli* that can accommodate high level expression of an exogenously introduced gene.

30

The proteins of the present invention can also be made by chemical synthesis. The principles of solid phase chemical synthesis of polypeptides are well known in the art and may be found in general texts relating to this area (Dugas, H. and Penney, C. 1981 *Bioorganic Chemistry*, pp 54-92, Springer-Verlag, New York). CEG polypeptides may  
5 be synthesized by solid-phase methodology utilizing an Applied Biosystems 430A peptide synthesizer (Applied Biosystems, Foster City, Calif.) and synthesis cycles supplied by Applied Biosystems. Protected amino acids, such as t-butoxycarbonyl-protected amino acids, and other reagents are commercially available from many chemical supply houses.

10

The polypeptides of the invention exhibit properties of a CEG protein, such as, for example, the ability to elicit the generation of antibodies that specifically bind an epitope associated with CEG polypeptides. Accordingly, the CEG polypeptide, or any oligopeptide thereof, is capable of inducing a specific immune response in appropriate  
15 animals or cells and binding with specific antibodies.

**C) ANTIBODIES THAT RECOGNIZE AND BIND THE PROTEINS AND POLYPEPTIDES OF THE INVENTION**

20 The invention further provides antibodies (e.g., polyclonal, monoclonal, chimeric, humanized, and human antibodies) that bind a CEG polypeptide. The most preferred antibodies will selectively bind a CEG polypeptide and will not bind (or will bind weakly) a non-CEG polypeptide. Antibodies that are particularly contemplated include monoclonal and polyclonal antibodies, as well as fragments thereof (e.g., recombinant proteins) which  
25 include the antigen binding domain and/or one or more complement determining regions of these antibodies. These antibodies can be from any source, for example, rabbit, sheep, rat, dog, cat, pig, horse, mouse, and human.

The invention encompasses antibody fragments that specifically recognize a CEG  
30 polypeptide. As used herein, an antibody fragment is defined as at least a portion of the variable region of the immunoglobulin molecule that binds to its target, i.e., the antigen binding region. Some of the constant region of the immunoglobulin may be included.

As will be understood by those skilled in the art, the regions or epitopes of a CEG polypeptide to which an antibody is directed may vary with the intended application. For example, antibodies intended for use in an immunoassay for the detection of membrane-bound CEG proteins on viable bacterial cells should be directed to an accessible epitope on membrane-bound CEG proteins. Antibodies that recognize other epitopes may be useful for the identification of CEG protein within damaged or dying cells, for the detection of secreted CEG protein or fragments thereof.

Various methods for the preparation of antibodies are well known in the art. For example, antibodies may be prepared by immunizing a suitable mammalian host using a CEG protein, peptide, or fragment, in isolated or immunoconjugated form (Harlow, 1989 *Antibodies*, Cold Spring Harbor Press, NY). In addition, fusion proteins comprising CEG polypeptides may also be used, such as a CEG protein/GST-fusion protein. Cells expressing or overexpressing a CEG polypeptide may also be used for immunizations. Similarly, any cell engineered to express CEG protein may be used. This strategy may result in the production of monoclonal antibodies with enhanced capacities for recognizing endogenous CEG protein.

The present invention contemplates chimeric antibodies that comprise a human and non-human immunoglobulin portion. The antigen combining region (variable region) of a chimeric antibody can be derived from a prokaryotic source (e.g., bacteria) and the constant region of the chimeric antibody which confers biological effector function to the immunoglobulin can be derived from a eukaryotic source (e.g., human). The chimeric antibody should have the antigen binding specificity of the prokaryotic antibody molecule and the effector function conferred by the eukaryotic antibody molecule.

In one example, the procedure used to produce chimeric antibodies can involve the following steps:

- a) Identifying and cloning the correct immunoglobulin gene segment encoding the antigen binding portion of the antibody molecule. This gene segment is known as the VDJ, variable, diversity and joining regions for heavy chains or VJ, variable,

joining regions for light chains or simply as the V or variable region. This gene regions may be in either the cDNA or genomic form;

- b) Cloning the gene segments encoding the constant region or desired part thereof;
- c) Ligating the variable region with the constant region so that the complete chimeric antibody is encoded in a form that can be transcribed and translated;
- d) Ligating this construct into a vector containing a selectable marker and gene control regions such as promoters, enhancers and poly(A) addition signals;
- e) Amplifying this construct in bacteria;
- f) Introducing this DNA into eukaryotic cells (transfection) most often mammalian lymphocytes;
- g) Selecting for cells expressing the selectable marker;
- h) Screening for cells expressing the desired chimeric antibody; and
- k) Testing the antibody for appropriate binding specificity and effector functions.

Chimeric antibodies of several distinct antigen binding specificities have been produced by protocols well known in the art, including anti-TNP antibodies (Boulianne et al., 1984 *Nature* 312:643); and anti-tumor antigen antibodies (Sahagan et al., 1986 *J. Immunol.* 137:1066). Likewise, several different effector functions have been achieved by linking new sequences to those encoding the antigen binding region. Examples of these include enzymes (Neuberger et al., 1984 *Nature* 312:604); immunoglobulin constant regions from another species and constant regions of another immunoglobulin chain (Sharon et al., 1984 *Nature* 309:364; Tan et al., 1985 *J. Immunol.* 135:3565-3567). Additionally, procedures for modifying antibody molecules and for producing chimeric antibody molecules using homologous recombination to target gene modification have been described (Fell et al., 1989 *Proc. Natl. Acad. Sci. USA* 86:8507-8511).

The predicted amino acid sequence of a CEG protein may be used to select specific regions of the CEG protein for generating antibodies. For example, hydrophobicity and hydrophilicity analyses of a CEG polypeptide may be used to identify hydrophobic and hydrophilic regions in the CEG protein. Regions of the CEG protein that show immunogenic structure, as well as other regions and domains, can readily be identified using

various other methods known in the art, such as Chou-Fasman, Garnier-Robson, Kyte-Doolittle, Eisenberg, Karplus-Schult or Jameson-Wolf analysis. Fragments that include the immunogenic regions are particularly suited for generating specific classes of antibodies.

- 5 Methods for preparing a protein for use as an immunogen and for preparing immunogenic conjugates of a protein with a carrier such as BSA, KLH, or other carrier proteins are well known in the art. In some circumstances, direct conjugation using, for example, carbodiimide reagents may be used; in other instances linking reagents such as those supplied by Pierce Chemical Co., Rockford, IL, may be effective. Administration of a CEG  
10 immunogen is conducted generally by injection over a suitable time period and with use of a suitable adjuvant, as is generally understood in the art. During the immunization schedule, titers of antibodies can be taken to determine adequacy of polyclonal antibody formation.

- While the polyclonal antisera produced in this way may be satisfactory for some  
15 applications, for pharmaceutical compositions, monoclonal antibody preparations are preferred. Immortalized cell lines which secrete a desired monoclonal antibody may be prepared using the standard method of Kohler and Milstein (*Nature* 256: 495-497) or other techniques as described in *Monoclonal Antibodies; A Manual of Techniques*, CRC press, Inc., Boca Raton, Fla. (1987) ed. Zola. The immortalized cell lines secreting the desired  
20 antibodies are screened by immunoassay in which the antigen is the CEG polypeptide having binding activity, or a fragment thereof. When the appropriate immortalized cell culture secreting the desired antibody is identified, the cells can be cultured either *in vitro* or by production in ascites fluid.

- 25 The desired monoclonal antibodies are then recovered from the culture supernatant or from the ascites supernatant. Fragments of the monoclonal antibodies of the invention or the polyclonal antisera (e.g., Fab, F(ab')<sub>2</sub>, Fv fragments, fusion proteins) which contain the immunologically significant portion (i.e., a portion that recognizes and binds a CEG protein) can be used as antagonists, as well as the intact antibodies. Humanized antibodies directed  
30 against a CEG polypeptide are also useful. The advantage of using humanized antibodies is that they are less immunogenic in humans. As used herein, a humanized antibody is an

immunoglobulin molecule which is capable of binding to a CEG polypeptide and which comprises a FR region having substantially the amino acid sequence of a human immunoglobulin and a CDR having substantially the amino acid sequence of non-human immunoglobulin or a sequence engineered to bind a CEG protein. Methods for humanizing  
5 murine and other non-human antibodies by substituting one or more of the non-human antibody CDRs for corresponding human antibody sequences are well known (Jones et al., 1986 *Nature* 321: 522-525; Riechman et al., 1988 *Nature* 332: 323-327; Verhoeyen et al., 1988 *Science* 239: 1534-1536; Carter et al., 1993 *Proc. Natl. Acad. Sci. USA* 89: 4285; and Sims et al., 1993 *J. Immunol.* 151: 2296).

10

Use of immunologically reactive fragments, such as the Fab, Fab', or F(ab')<sub>2</sub> fragments is often preferable, especially in a therapeutic context, as these fragments are generally less immunogenic than the whole immunoglobulin. Further, bi-specific antibodies specific for two or more epitopes may be generated using methods generally known in the art. Further,  
15 antibody effector functions may be modified so as to enhance the therapeutic effect of the antibodies of the invention. For example, cysteine residues may be engineered into the Fc region, permitting the formation of interchain disulfide bonds and the generation of homodimers which may have enhanced capacities for internalization, ADCC and/or complement-mediated cell killing (Caron et al., 1992 *J. Exp. Med.* 176: 1191-1195; Shopes, 1992 *J. Immunol.* 148: 2918-2922). Homodimeric antibodies may also be  
20 generated by cross-linking techniques known in the art (Wolff et al., *Cancer Res.* 53: 2560-2565). The invention also provides pharmaceutical compositions having the monoclonal antibodies or anti-idiotypic monoclonal antibodies of the invention.

25 The antibodies or fragments may also be produced, using current technology, by recombinant means. Regions that bind specifically to the desired regions of the CEG protein can also be produced in the context of chimeric or CDR grafted antibodies of multiple species origin. The invention includes an antibody, e.g., a monoclonal antibody which competitively inhibits the immunospecific binding of any of the monoclonal  
30 antibodies of the invention to a CEG protein.



Alternatively, methods for producing fully human monoclonal antibodies, include phage display and transgenic methods, are known and may be used for the generation of human monoclonal antibodies (reviewed in: Vaughan et al., 1998 *Nature Biotechnology* 16: 535-539). For example, fully human monoclonal antibodies may be generated using cloning technologies employing large human Ig gene combinatorial libraries (i.e., phage display) (Griffiths and Hoogenboom, "Building an *in vitro* immune system: human antibodies from phage display libraries", in: *Protein Engineering of Antibody Molecules for Prophylactic and Therapeutic Applications in Man*, Clark, M. (Ed.), Nottingham Academic, pp 45-64 (1993); Burton and Barbas, "Human Antibodies from combinatorial libraries" *Id.*, pp 65-82). Fully human monoclonal antibodies may also be produced using transgenic mice engineered to contain human immunoglobulin gene loci as described in PCT Patent Application WO98/24893, Jakobovits et al., published December 3, 1997 (see also, Jakobovits, 1998 *Exp. Opin. Invest. Drugs* 7: 607-614). This method avoids the *in vitro* manipulation required with phage display technology and efficiently produces high affinity, authentic human antibodies.

The antibody or fragment thereof of the invention may be labeled with a detectable marker or conjugated to a second molecule, such as a therapeutic agent (e.g., a cytotoxic agent) thereby resulting in an immunoconjugate. For example, the therapeutic agent includes, but is not limited to, an anti-tumor drug, a toxin, a radioactive agent, a cytokine, a second antibody or an enzyme. Further, the invention provides an embodiment wherein the antibody of the invention is linked to an enzyme that converts a prodrug into a cytotoxic drug.

Examples of cytotoxic agents include, but are not limited to ricin, ricin A-chain, doxorubicin, daunorubicin, taxol, ethidium bromide, mitomycin, etoposide, teniposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphtheria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, arbrin A chain, modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, sapaonaria officinalis inhibitor, and glucocorticoid and other chemotherapeutic agents, as well as radioisotopes such as  $^{212}\text{Bi}$ ,  $^{131}\text{I}$ ,  $^{131}\text{In}$ ,  $^{90}\text{Y}$ , and  $^{186}\text{Re}$ .

Suitable detectable markers for diagnostic used include, but are not limited to, a radioisotope, a fluorescent compound, a bioluminescent compound, chemiluminescent compound, a metal chelator or an enzyme. Antibodies may also be conjugated to an anti-  
5 cancer pro-drug activating enzyme capable of converting the pro-drug to its active form. See, for example, U.S. Patent Nos. 4,952,394 and 5,716,990.

Additionally, a recombinant protein of the invention comprising the antigen-binding region of any of the monoclonal antibodies of the invention can be made. In such a  
10 situation, the antigen-binding region of the recombinant protein is joined to at least a functionally active portion of a second protein having therapeutic activity. The second protein can include, but is not limited to, an enzyme, lymphokine, oncostatin or toxin. Suitable toxins include those described above.

15 Techniques for conjugating or joining therapeutic agents to antibodies are well known (Arnon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy", in: *Monoclonal Antibodies And Cancer Therapy*, Reisfeld et al. (eds.), pp. 243-56, Alan R. Liss, Inc. 1985; Hellstrom et al., "Antibodies For Drug Delivery", in: *Controlled Drug Delivery* (2nd Ed.), Robinson et al. (eds.), pp. 623-53, Marcel Dekker, Inc. 1987; Thorpe,  
20 "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in: *Monoclonal Antibodies '84: Biological And Clinical Applications*, Pinchera et al. (eds.), pp. 475-506 (1985); and Thorpe et al., "The Preparation And Cytotoxic Properties Of Antibody-Toxin Conjugates", in: *Immunol. Rev.*, 62:119-58 (1982)). Techniques for joining detectable markers to antibodies are also known.

25

#### **D) PHARMACEUTICAL COMPOSITIONS OF THE INVENTION**

The invention includes pharmaceutical compositions for use in the treatment of microbial infections comprising a pharmaceutically effective amount of an anti-CEG antibody or a  
30 CEG polypeptide.

In one embodiment, the pharmaceutical compositions may comprise a CEG antibody, either unmodified, conjugated to a therapeutic agent (e.g., drug, toxin, enzyme or second antibody) or in a recombinant form (e.g., chimeric or bispecific). The compositions may additionally include other antibodies or conjugates (e.g., an antibody cocktail).

5

The pharmaceutical compositions also preferably include suitable carriers and adjuvants which include any material which when combined with the molecule of the invention (e.g., an anti-CEG antibody or a CEG protein) retains the molecule's activity and is non-reactive with the subject's immune systems. Examples of suitable carriers and adjuvants include, but are not limited to, human serum albumin, ion exchangers, alumina, lecithin, buffer substances such as phosphates, glycine, sorbic acid, potassium sorbate, and salts or electrolytes such as protamine sulfate. Other examples include any of the standard pharmaceutical carriers such as a phosphate buffered saline solution, water, emulsions such as oil/water emulsion, and various types of wetting agents. Other carriers may also include sterile solutions, tablets including coated tablets and capsules. Typically such carriers contain excipients such as starch, milk, sugar, certain types of clay, gelatin, stearic acid or salts thereof, magnesium or calcium stearate, talc, vegetable fats or oils, gums, glycols, or other known excipients. Such carriers may also include flavor and color additives or other ingredients. Compositions comprising such carriers are formulated by well known conventional methods. Such compositions may also be formulated within various lipid compositions, such as, for example, liposomes as well as in various polymeric compositions, such as polymer microspheres.

The pharmaceutical compositions of the invention can be administered using conventional modes of administration including, but not limited to, intravenous, intraperitoneal, oral, intralymphatic or administration directly into the tumor. Intravenous administration is preferred.

The pharmaceutical compositions of the invention may be in a variety of dosage forms which include, but are not limited to, liquid solutions or suspensions, tablets, pills, powders, suppositories, polymeric microcapsules or microvesicles, liposomes, and

injectable or infusible solutions. The preferred form depends upon the mode of administration and the therapeutic application.

5 The CEG polypeptides and proteins of this invention are found in common pathogenic bacterial species such as *Streptococcus pneumoniae*. This organism causes upper respiratory tract infections. Thus, the peptides and proteins of this invention can be used as immunogens in subunit vaccines for vaccination against a pathogenic bacteria such as *Streptococcus pneumoniae*. Additionally, the *ceg* sequences of the invention can be used as DNA vaccines (U.S. Patent No. 5,736,524 and U.S. Patent No. 5,989,553).

10

The polypeptides and proteins of this invention can be formulated as univalent and multivalent vaccines. The protein can be mixed, conjugated or fused with other antigens, including B or T cell epitopes of other antigens.

15 Further, when a haptenic peptide of the proteins of the invention is used, (i.e., a peptide which reacts with cognate antibodies, but cannot itself elicit an immune response), it can be conjugated to an immunogenic carrier molecule. Conjugation to an immunogenic carrier can render the oligopeptide immunogenic. Examples of carrier molecules are tetanus toxin or toxoid, diphtheria toxin or toxoid and any mutant forms of these proteins  
20 such as CRM.sub.197. Others include exotoxin A of *Pseudomonas*, the heat labile toxin of *E. coli* and rotaviral particles (including rotavirus and VP6 particles). Alternatively, a fragment or epitope of the carrier protein or other immunogenic protein can be used. For example, the hapten can be coupled to a T cell epitope of a bacterial toxin.

25 In formulating the vaccine compositions with the CEG polypeptides or proteins of the invention, alone or in the various combinations described, the immunogen is adjusted to an appropriate concentration and formulated with any suitable vaccine adjuvant. Suitable adjuvants include, but are not limited to: surface active substances, e.g., hexadecylamine, octadecylamine, octadecyl amino acid esters, lysolecithin, dimethyl-  
30 dioctadecylammonium bromide), methoxyhexadecylglycerol, and pluronic polyols; polyamines, e.g., pyran, dextran sulfate, poly. IC, carbopol; peptides, e.g., muramyl

dipeptide, dimethylglycine, tuftsin; oil emulsions; and mineral gels, e.g., aluminum hydroxide, aluminum phosphate, etc. and immune stimulating complexes. The immunogen may also be incorporated into liposomes, or conjugated to polysaccharides and/or other polymers.

5

The vaccines can be administered to a human or animal in a variety of ways. These include intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, oral and intranasal routes of administration. Further, the vaccines can be live or inactivated vaccines.

10

The most effective mode of administration and dosage regimen for the compositions of this invention depends upon the severity and course of the disease, the patient's health and response to treatment and the judgment of the treating physician. Accordingly, the dosages of the compositions should be titrated to the individual patient.

15

#### E) USES OF THE MOLECULES OF THE INVENTION

##### 1) MOLECULAR WEIGHT MARKERS

20 The nucleic acid molecules of the invention and their encoded proteins may be employed as molecular weight markers. For example, the molecular weight of each of the nucleic acid molecules having *ceg* sequences and their predicted polypeptides can be determined and can be used to compare against other gene sequences and proteins whose molecular weights are unknown.

25

##### 2) DIAGNOSTICS

The nucleic acid molecules of the invention may be employed in diagnostic embodiments. For example, the presence of nucleotide sequences which are identical or  
30 similar to the *ceg* sequences of the invention may be detected within a biological sample.

The biological sample may include blood, serum or a swab from nose, ear or throat, may be determined by means of a nucleic acid detection assay.

5 Nucleic acid probes or primers having sequences complementary to *ceg* sequences may be used in a hybridization assay to detect the presence of the sequences which are identical or similar to the *ceg* sequences of the invention in the biological samples. Typically, nucleic acids molecules obtained from a suitable biological sample are hybridized with labeled probes or primers. The resulting hybridized molecules are detected and resolved by methods well known in the art, such as Northern or Southern  
10 blotting, micro-array technology, or amplifying with PCR technology. Other hybridization techniques and systems are known that can be used in connection with the detection aspects of the invention, including diagnostic assays such as those described in Falkow et al., U.S. Pat. No. 4,358,535.

15 Examples of the PCR technology are disclosed in U.S. Patent Nos. 4,683,202 and 4,965,188 (incorporated herein by reference). Generally, nucleic acid molecules are obtained from a suitable biological source and contacted with two primers corresponding to the *ceg* sequences disclosed herein, under conditions which allow for hybridization and polymerization to occur. A pair of probes, one corresponding to the 5' flanking region and the other corresponding to the 3' flanking region, would be sufficient to detect the  
20 nucleic acid molecules of the invention in a biological sample and may be used to indicate the amount of bacteria present.

Alternative methods of detecting nucleic acid molecules include, for example, in situ  
25 hybridization techniques, where a *ceg* probe is used to detect homologous sequences within one or more cells, such as cells within a clinical sample or even cells grown in tissue culture. As is well known in the art, the cells are prepared for hybridization by fixation, e.g. chemical fixation, and placed in conditions that allow for the hybridization of a detectable probe with nucleic acids located within the fixed cell.

30

The amount of *ceg* sequences present in a biological sample can be quantified and compared to the levels in a normal or "healthy" sample. For example, *ceg* sequences present in either increased or decreased levels, compared to the levels found in the control sample may indicate the presence of bacteria. This information is useful for  
5 diagnosis of a bacterial infection that requires treatment with an antibacterial agent.

Alternatively, the amount of CEG polypeptides present in a biological sample may be determined by means of an immunoassay. For example, labeled antibodies reactive against CEG polypeptides may be used in an immuno-reactive assay to detect the  
10 presence of CEG polypeptides in the biological samples.

### 3) SCREENING CANDIDATE CEG SEQUENCES

#### a) Gene Disruption Assay

15

The *ceg* nucleotide sequences of the invention can be used to identify nucleotide sequences which are identical or similar to the *ceg* sequences that are required for bacterial cell viability. For example, the *ceg* sequences can be used in a bacterial gene disruption assay to screen candidate nucleotide sequences to identify sequences required  
20 for bacterial cell viability.

The disruption assay can involve: introducing into a host cell a recombinant vector that is capable of integration into the host genome, where the recombinant vector includes a candidate sequence that putatively encodes a cell-viability gene product (e.g., the  
25 exogenous *ceg* sequence); the vector integrates the candidate sequence into a target sequence within the host's genome (e.g., the endogenous *ceg* sequence); and the host cell, so introduced, is screened for viability. The recombinant vector preferably includes a selectable marker so that the introduced host cell can be screened for viability in the presence of a selectable agent.

30

For example, Figure 1 shows a schematic representation of a gene disruption assay, within a bacterial host cell. In Figure 1A, the recombinant vector, pEVP3, includes the CAT gene (e.g., the selectable marker chloramphenicol acetyl transferase) and an internal region of the *ceg* disrupting sequence; the internal region excludes the 5' and 3' ends of the *ceg* sequence. The "X" in Figure 1 indicates the recombinant pEVP3 vector undergoing homologous recombination with the target sequence (e.g., within the host genome). In Figure 1B, the resolved pEVP3 vector that is integrated into the host genome, is shown. Left to right are the following elements: the native promoter of the target gene; a 5' partial copy of the target gene; the body of the integrated pEVP3 vector including the disrupting gene and CAT; and, a 3' partial copy of the target gene. Thus, integration of the pEVP3 vector via homologous recombination results in two partial gene duplications flanking the integrated vector. If the target gene is not essential for survival, it is possible to recover chloramphenicol-resistant colonies of *S. pneumoniae*. Failure to recover chloramphenicol resistant colonies, in the presence of the proper controls as described below, indicates that the target gene may be essential for cell viability.

More particularly, the gene disruption assay for screening candidate *ceg* sequences can involve the following steps. The recombinant pEVP-3 vector encoding CAT resistance and having a fragment of a candidate *ceg* sequence, can be introduced into transformation-competent *S. pneumoniae* cells by methods that are well-known in the art (Lee, M.S., et al., 1998 *Appl. Environ. Microbiol.* 64:4796-4802). The preferred size of the *ceg* fragment can be between about 200 to about 500 bp in length. It is advantageous that the candidate *ceg* sequence does not include the 5' and 3' ends that encode the N- and C-terminal ends of the CEG polypeptide. This insures that the inserted *ceg* fragment and the disrupted endogenous *ceg* gene sequence are not capable of expression of a full-length, functional *ceg* gene product. The transformation-competent cells can be obtained by performing the transformation step in the presence of a heptadecapeptide that induces competence for transformation of *S. pneumoniae* (Havarstein, L. S., et al., 1995 *Proc. Nat'l. Acad. Sci.* 92:11140-11144), such as the CSP-1 peptide. The CSP-1 can be naturally-derived or synthetic. Additionally, the transformation step can be optimized by performing the transformation when the cells have reached a density which is optimal for



transformation (e.g.,  $3 \times 10^7$  cells per ml.) (Havarstein, L. S. et al. *supra*). The recombinant vector can be introduced into the competent pneumococci and may undergo homologous recombination, whereby the candidate *ceg* fragment recombines with the corresponding endogenous *ceg* sequence, resulting in targeted integration of the vector into the pneumococcal genome and disruption of the endogenous *ceg*.

The transformed cells can be plated on or cultured in chloramphenicol-containing growth medium. The cells can be cultured under standard conditions, such as 37° C in 5% CO<sub>2</sub> for approximately 40 to 48 hours, for the purpose of selecting cells that carry the integrated vector.

Additionally, control samples can be run in parallel with the gene disruption assay, in order to determine whether the gene disruption procedure is working properly. For example, the control samples can be used to calibrate the gene disruption experiment so that disruption of a known non-essential bacterial gene results in an approximate number of colonies per plate. Similarly, the disruption of a known essential gene can be calibrated to yield only zero or one colony per plate. The appearance of one colony is due to the rare illegitimate recombination into a non-homologous sequence. In particular, a known non-essential gene such as the *lytA* gene (Tomasz, A., et al., 1988 *J. Bacteriol.* 170:5931-5934) can be used so that between about 70 to 100 chloramphenicol-resistant colonies will grow per plate. Similarly, the *ftsZ* gene (Lutkenhaus, J. F., et al., 1980 *J. Bacteriol.* 143:1281-1288), a known essential gene, can be used to yield zero or, rarely, one colony per plate. As is well known in the art, specific parameters that are involved in any given gene disruption assay can be adjusted to calibrate the desired number of plated cells in the control samples. Experimental parameters that can be adjusted include, but are not limited to, the *E. coli* strain used to propagate the vector/insert, the fragment length of the sequence to be integrated, the amount of recombinant integration vector used to transform the cells, use of transformation-competent cells, and plating density of the transformed cells.

The transformed cells carrying the recombinant integration vector that disrupts expression of an endogenous essential gene (e.g., the target *ceg* gene) can be identified, based on a selectable phenotype such as non-viability. For example, the cells that carry a disrupted non-essential gene will be viable and, due to the integration of pEVP3, will grow on chloramphenicol-containing medium. In contrast, cells that carry a disrupted essential gene will not grow (e.g., non-viable) on the chloramphenicol-containing medium. Thus, the transformed cells that do not grow under these selective conditions carry an endogenous gene sequence that is essential for cell viability which has been disrupted by an exogenous candidate fragment, thereby identifying a *ceg* sequence. Steps one through three may be repeated in order to confirm that the *ceg* sequences, so identified, are essential for cell viability.

#### b) Autolysin Assay

It is advantageous to perform additional steps to determine whether the homologous recombination events result in disruption of the intended target gene sequence. The *lytA* transformation control can be used to confirm that the transformation system is functioning properly. For example, a phenotypic test for autolysin activity (*lytA* gene product) can be performed to determine that the exogenous *lytA* fragment is correctly integrated into the *lytA* site within the host genome. This typically involves flooding the culture plates containing transformants carrying the integrated *lytA* control vector with a solution of detergent, such as 0.1% deoxycholate, which triggers cell lysis in *lytA*-intact cells (e.g., the cells that have not undergone homologous recombination). After about 5-10 minutes the colonies with intact *lytA* will appear ghost-like due to cell lysis, and the colonies with a disrupted *lytA* gene will appear intact.

#### c) Polarity Analysis

The *ceg* sequences that are confirmed to be essential for cell viability can be examined further by performing a polarity analysis to determine if the corresponding endogenous *ceg* sequence is organized in an operon. Polarity is an effect unique to prokaryotes and is

the result of the operon organization of bacterial genomes. Many bacterial genes are arranged in operons in which multiple genes are under the control of a single regulatory sequence (e.g., a promoter) and are transcribed into a single mRNA transcript. With respect to the orientation of multiple genes within an operon, the genes that are proximal to the regulatory sequence are said to be "upstream" genes and the genes that are distal are said to be "downstream" genes. For example, many operons contain genes encoding different proteins that catalyze discrete steps of a common biochemical pathway. Thus, any of the proteins that catalyze the steps of the pathway may be essential for cell viability.

10

The presence of operons in a bacterial host genome may influence the interpretations of the gene disruption results. For example, disruption of an upstream gene may be erroneously interpreted as affecting the expression of the disrupted gene but may, in fact, have expression effects on the intact downstream genes. Therefore, it is advantageous to perform a polarity analysis to determine if a *ceg* sequence is part of an operon.

15

A polarity analysis can involve performing an *in vivo* gene disruption procedure using, as the disrupting sequence, a *ceg* sequence that includes the entire *ceg* coding sequence region but lacking expression regulatory sequences. This differs from the gene disruption assay, which involves the central region of the *ceg* sequence. The polarity analysis involves gene duplication via homologous recombination. For example, the pEVP-3 vector having the entire coding region of a *ceg* sequence can be used for the polarity analysis (Figure 2 A). The polarity analysis will yield different results depending on the organization of the endogenous target sequence within the host genome.

20

For example, Figure 2 shows a schematic representation of the polarity test for operons, within a bacterial host cell. In Figure 2A, the recombinant vector, pEVP3, includes the CAT gene and the entire coding region of the *ceg* disrupting sequence. The "X" in Figure 2 indicates the recombinant pEVP3 vector undergoing homologous recombination with the target sequence. Two of the possible results of homologous recombination are shown in Figures 2 B and C.

25

30

In Figure 2 B, case 1, if the endogenous target sequence is not organized in an operon, the integration event may yield: a functional target sequence (e.g., it is capable of expression); a duplicate non-functional target sequence that lacks a promoter; and a functional downstream gene (e.g., Gene B) that is controlled by its own promoter. The cells carrying this type of integrated target sequence can be recovered as viable cells that grow in the presence of chloramphenicol; this condition is termed "polarity negative".

In Figure 2 C, case 2, if the target sequence is organized in an operon, then the integration event may yield an integration site that is similar to that described for case 1, including: a functional target sequence; and a duplicate non-functional target sequence which is not functional. However, this integration event may also yield a non-functional downstream gene (e.g., Gene B) because expression of this downstream gene is controlled by a promoter located upstream of the insertion site. The cells that carry this type of integrated target sequence will be non-viable; this condition is termed "polarity positive". Thus, the polarity analysis provides a method to determine whether integration of a recombinant vector into a target *ceg* sequence effects expression of downstream genes.

The *ceg* sequences disclosed herein (SEQ ID NOs.: 1-113, 227-331) encode gene products that are essential for viability in *S. pneumoniae*. Furthermore, many of these *ceg* sequences have been analyzed for the polarity effect and the results are presented in Table I. One subset of *ceg* sequences is classified as polarity negative (-), since the homologous recombination event did not effect the expression of downstream genes. Another subset of *ceg* sequences is classified as polarity positive (+), since the homologous recombination event did affect the expression of downstream genes. The *ceg* sequences that have not yet been classified as polarity positive or negative are indicated in Table I as a blank. For the *ceg* sequences that are classified as polarity positive, the genes downstream of the disrupted endogenous *ceg* sequences may or may not also be essential.

#### 4) ASSAYS FOR IDENTIFYING CEG LIGANDS AND OTHER BINDING AGENTS

- The present invention provides screening methods for identifying agents that interact and/or bind to the CEG proteins of the invention, such as a ligand. An agent can be, for example, a natural product, a derived or synthetic chemical molecule, a polypeptide, a nucleic acid molecule, or a metal. The agents that interact with CEG proteins may cause bacterial cell death by disrupting the functions of CEG proteins, including, but not limited to, nucleotide biosynthesis, DNA replication, RNA transcription, protein translation, and/or cell wall biosynthesis. Accordingly, the present invention provides screening methods for identifying agents having antibacterial activity, such as agents that cause bacterial cell death by interacting with the CEG proteins. These antibacterial agents are useful for treating diseases and afflictions associated with bacterial infections.
- Various methods can be used to discover agents having antibacterial activity, as determined by the ability of the binding agent to bind to a CEG protein and disrupt the function of the CEG protein. These screening methods include whole cell *in vivo* assays as well as *in vitro* assays with cellular components.
- An *in vivo* screening method for identifying ligands that bind CEG polypeptides can be performed in a whole cell assay. A typical method may be the use of whole bacterial cells to assess the antibacterial properties based on cell growth or viability. These methods can include methods for measuring cell growth and/or viability, for example, by optical density or zones of growth (Koch, A. L. et al., 1970 *Anal. Biochem.* 38:252-259; Biemer, J. J. et al., 1973 *Ann. Clin. Lab. Sci.* 2:135-140; *Manual of Clinical Microbiology*, 7<sup>th</sup> edition, Murray, P. R. (ed), ASM Press), by growth inhibition in an agar assay (Murray, P. R., *supra*), or other means of detecting cell metabolism (Mychajlonka, M. et al., 1980 *Antimicrob. Agents Chemother.* 17:572-582), and are well known to those skilled in the art. In addition, there are molecular biology-based detection methods for use with whole bacterial cells, such as gene reporter assays, to monitor the effect of the ligand on specific targets (Slauch, J. M., et al., 1991 *Methods Enzymol.* 204:213-248). Examples of the reporter genes include, but are not limited to, beta-

galactosidase, alkaline phosphatase, luciferase, and green fluorescent protein. For example, one embodiment provides a reporter system that monitors inhibition of DNA synthesis by fusing a reporter such as beta-galactosidase (*lacZ*) to genes known to be upregulated by the cessation of DNA synthesis as a result of the binding of ligands to the DNA synthetic apparatus. (Shurvinton, C. E., et al., 1982 *Mol. Gen. Genetics* 185:352-355; Rosato, A., et al., 1998 *Antimicrob. Agents Chemother.* 42:1392-1396).

Alternatively, the yeast two-hybrid system (Fields, S. and Song, O. 1989, *Nature* 340:245-246) may be adapted to screen for ligands that bind CEG polypeptides. Generally, the yeast two-hybrid system is performed in a yeast host cell carrying a reporter gene, and is based on the modular nature of the GAL transcription factor which has a DNA binding domain and a transcriptional activation domain. The yeast two-hybrid system relies on the physical interaction between a recombinant polypeptide that comprises the GAL DNA binding domain and another recombinant polypeptide that comprises the GAL transcriptional activation domain. The physical interaction between the two recombinant polypeptides reconstitutes the transcriptional activity of the transcription factor, thereby causing expression of the reporter gene. Either of the recombinant polypeptides used in the two-hybrid system can be generated to include a CEG polypeptide sequence to screen for binding partners of CEG.

Another method uses the bacterial CEG proteins as the basis for *in vitro* assay systems to detect binding agents. Typically, the *in vitro* screening method comprises: a) generating the CEG protein of the invention, or membranes enriched in the CEG protein; b) exposing the CEG protein or membranes to a candidate agent; and c) detecting the interaction of the CEG protein with the agent by any suitable means. Additionally, the screening methods may be adapted to automated high-throughput procedures, such as PANDEX.RTM Baxter-Dade Diagnostics, allowing for efficient high-volume screening of candidate agents.

An alternative method for screening potential ligands involves an *in vitro* binding procedure. Typically, the CEG proteins of the invention can be produced using

recombinant DNA technology and host-vector systems as described herein. A candidate agent is introduced into a reaction vessel containing the CEG protein, or fragment thereof; the candidate agents may be detectable by methods such as, but not limited to, radioisotope or chemical labeling. Binding of the CEG protein by a candidate agent can  
5 be determined by any suitable means, including, for example, quantifying bound label versus unbound label using any suitable method. Binding of a candidate agent may also be detected by methods similar to an alternative physical method disclosed in U.S. Patent No. 5,585,277. In this method, binding of a candidate agent to a protein is assessed by monitoring the ratio of folded protein to unfolded protein, for example by monitoring  
10 sensitivity of the protein to a protease, or amenability to binding of the protein by a specific antibody against the folded state of the protein, or binding to chaperone protein, or by binding to any suitable surface.

The invention provides methods of identifying compounds that modulate (e.g., activate or  
15 inhibit) the function of a CEG polypeptide. Essentially any compound can be used in the assays of the invention. The preferred compounds are those that are soluble in aqueous or organic solutions. It will be appreciated by those of skill in the art that there are many commercial suppliers of chemical compounds that can be used in the methods of the invention, including Sigma Chemical Co. (St. Louis, Mo.), Aldrich Chemical Co. (St.  
20 Louis, Mo.), Sigma-Aldrich (St. Louis, Mo.), Fluka Chemika-Biochemica Analytika (Buchs, Switzerland), and the like.

The present invention provides methods for detecting compounds which are identified as modulators of CEG function. The methods of the invention can be performed using  
25 isolated CEG polypeptides, or use whole cells expressing the CEG polypeptide. The steps of the method using isolated CEG polypeptides include: contacting the isolated CEG polypeptide with a candidate compound; and determining whether the function of the CEG polypeptide is altered. The steps of the method using whole cells include: contacting the whole cells with a candidate compound; and determining whether the cell  
30 dies, indicating the compound inhibited the function of a CEG polypeptide.

The preferred methods of the invention provide high-throughput screening assays for identifying compounds which modulate the function of a CEG polypeptide. The high throughput methods permit screening of large libraries of compounds. For example the high throughput methods can use automated assay steps. The assays can be performed  
5 in parallel on a solid support, as microtiter formats on microtiter plates in robotic assays are well known. A preferred embodiment of the methods includes adapting the methods to use microtiter plates or pico- nano- or micro-liter arrays. In high throughput assays it is desirable to run positive controls to ensure that the components of the assays are working properly.

10 The high throughput screening methods of the invention include providing a combinatorial library containing a large number of compounds (candidate modulator compounds) (Borman, S. C. & E. News, 1999, 70(10), 33-48). Such combinatorial chemical libraries can be screened in one or more assays to identify library members  
15 (particular chemical species or subclasses) that exhibit the ability to modulate the function of the CEG polypeptide (Borman, S., *supra*; Dagani, R. C. & E. News, 1999, 70(10), 51-60). The compounds, so identified, can serve as lead-compounds or can themselves be used as potential or actual therapeutics.

20 A combinatorial chemical library is a collection of diverse chemical compounds generated by using either chemical synthesis or biological synthesis, to combine a number of chemical building blocks, such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide library, is formed by combining a set of chemical building blocks (amino acids) in every possible way for a given  
25 compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in  
30 the art. Such combinatorial chemical libraries include, but are not limited to, peptide libraries (see, e.g., U.S. Pat. No. 5,010,175, Furka, *Int. J. Pept. Prot. Res.*, 1991, 37:487-493 and



Houghton, et al., *Nature*, 1991, 354, 84-88). Other chemistries for generating chemical diversity libraries can also be used. Such chemistries include, but are not limited to, peptoids (PCT Publication No. WO 91/19735); encoded peptides (PCT Publication WO 93/20242); random bio-oligomers (PCT Publication No. WO 92/00091); benzodiazepines (U.S. Pat. No. 5,288,514); diversomers, such as hydantoins, benzodiazepines and dipeptides (Hobbs, et al., *Proc. Nat. Acad. Sci. USA*, 1993, 90, 6909-6913); vinylogous polypeptides (Hagihara, et al., *J. Amer. Chem. Soc.*, 1992, 114, 6568); nonpeptidal peptidomimetics with *beta*-D-glucose scaffolding (Hirschmann, et al., *J. Amer. Chem. Soc.*, 1992, 114, 9217-9218); analogous organic syntheses of small compound libraries (Chen, et al., *J. Amer. Chem. Soc.*, 1994, 116, 2661; Armstrong, et al. *Acc. Chem. Res.*, 1996, 29, 123-131); or small organic molecule libraries (see, e.g., benzodiazepines, Baum *C&E News*, 1993, Jan. 18, page 33,); oligocarbamates (Cho, et al., *Science*, 1993, 261, 1303); and/or peptidyl phosphonates (Campbell, et al., *J. Org. Chem.* 1994, 59, 658); nucleic acid libraries (see, Seliger, H et al., *Nucleosides & Nucleotides*, 1997, 16, 703-710); peptide nucleic acid libraries (see, e.g., U.S. Pat. No. 5,539,083); antibody libraries (see, e.g., Vaughn, et al., *Nature Biotechnology*, 1996, 14(3), 309-314 and PCT/US96/10287); carbohydrate libraries (see, e.g., Liang, et al., *Science*, 1996, 274, 1520-1522 and U.S. Pat. No. 5,593,853, Nilsson, UJ, et al., *Combinatorial Chemistry & High Throughput Screening*, 1999 2, 335-352; Schweizer, F; Hindsgaul, O. *Current Opinion In Chemical Biology*, 1999 3, 291-298); isoprenoids (U.S. Pat. No. 5,569,588); thiazolidinones and metathiazanones (U.S. Pat. No. 5,549,974); pyrrolidines (U.S. Pat. Nos. 5,525,735 and 5,519,134); morpholino compounds (U.S. Pat. No. 5,506,337); benzodiazepines (U.S. Pat. No. 5,288,514); and other similar art.

Devices for the preparation of combinatorial libraries are commercially available (see, e.g., 357 MPS, 390 MPS, Advanced Chem. Tech, Louisville Ky., Symphony, Rainin, Woburn, Mass., 433A Applied Biosystems, Foster City, Calif., 9050 Plus, Millipore, Bedford, Mass.). In addition, numerous combinatorial libraries are themselves commercially available (see, e.g., ComGenex, Princeton, N.J., Asinex, Moscow, Ru, Tripos, Inc., St. Louis, Mo., ChemStar, Ltd., Moscow, RU, 3D Pharmaceuticals, Exton, Pa., Martek Bio sciences, Columbia, Md., etc.).

In the high throughput methods of the invention, several thousand different candidate compounds can be screened in a relatively short period of time. For example, each well of a microtiter plate can be used to run a separate assay against a selected potential modulator, or if concentration or incubation time effects are to be observed, every 5-10 wells can test a single modulator. Thus, a single standard microtiter plate can assay about 100 (96) modulators. If 1536 well plates are used, then a single plate can easily assay from about 100 to about 1500 different compounds. It is possible to assay many different plates per day; assay screens for up to about 6,000-20,000, and even up to about 100,000-1,000,000 different candidate modulator compounds are possible using the methods of the invention.

The following examples are presented to illustrate the present invention and to assist one of ordinary skill in making and using the same. The examples are not intended in any way to otherwise limit the scope of the invention.

#### EXAMPLE 1

The following provides a general description of how a list of candidate *ceg* sequences was generated. The list was generated by selecting candidate *ceg* gene sequences from a Concordance web engine using the method described in: Brucoleri, R.E., Dougherty, T.J., Davison, D.B. (1998) "Concordance analysis of microbial genomes" in: *Nucleic Acids Res* 26:4482-4486.

#### Microbial Genomics CEG Discovery Process Summary.

##### Microbial Concordance Analysis

The entire genomic sequence data of various bacteria was acquired from several public and proprietary sequence database sources, including GTC (Genome Therapeutics Corporation), and TIGR (The Institute for Genomic Research).

Predicted ORFs from the genomic data were identified, translated, and stored. The desirable ORFs were at least 90 amino acid residues in length. Concordance analysis was performed among bacteria and various parameters were used to filter out genes with high similarity to eukaryotes.

5

#### Concordance Analysis

The entire genomic sequence of various Eubacteria was acquired from several public and private sources. The proprietary PathoGenome System from Genome Therapeutics Corporation, Waltham, MA, USA contributed data. Public data was obtained from  
10 GenBank (<http://ncbi.nlm.nih.gov>), The Institute for Genomic Research (TIGR), the Yeast Proteome Database, from Proteome, Inc. of Beverly, MA, and the Sanger Center of the Medical Research Council of the United Kingdom (<http://www.sanger.ac.uk>). Additionally, the non-microbial sequence data used as a basis for comparison and data  
15 subtraction was obtained from a proprietary database, including the LifeSeq Database from Incyte Pharmaceuticals, Palo Alto, CA.

Where required, Incyte nucleotide sequences were translated into protein sequences in all six possible reading frames. GTC supplied predicted protein sequences with their data. In  
20 the case of other eubacterial nucleotide sequences, the program CRITICA (Badger, J. and Olsen, G., 1999 "CRITICA: coding region identification tool invoking comparative analysis" in: *Molecular Biology and Evolution* 16:512-524). The sequences were stored in flat files on a Unix computer system. Each predicted amino acid sequence had to be greater than 90 amino acids.

25

Each predicted protein sequence was compared to every other sequence (an "all-against-all" comparison). The program used was FASTA (Pearson, W.R., "Flexible sequence similarity searching with the FASTA3 program package." *Methods in Molecular Biology* 2000 132:185-219.) The parameters used were ktup=2, and all scores above the default  
30 cutoff were kept. The output was processed and stored in a PostGres 95 database (<http://www.postgresql.org>). Graphical user interfaces, using web browser technology, were constructed to query the database.

A Concordance Analysis was performed on the data. The question used to generate the dataset was show all *Streptococcus pneumoniae* open reading frames with a similarity  
5 greater than or equal to 30% overall protein sequence identity to both selected gram-positive and/or gram-negative bacteria in the database. The data was further required not to match yeast or human sequences at greater than 30% overall protein sequence similarity. The resulting dataset included a list of more than 400 conserved amino acid sequences having known or unknown function. The amino acid sequences having  
10 unknown functions formed the basis of a list designated Conserved Unknown Reading Frames, or CURFs which is a subset of the total list of CEGs (e.g., CURFs includes known and unknown).

The resulting list of conserved genes (e.g., more than 400 sequences) was used as a basis  
15 for selecting and screening bacterial gene sequences that are essential for cell viability. The Concordance system was designed to permit high-throughput identification of conserved gene sequences in the database. (Brucoleri, R, Dougherty, T, and Davison, D. 1998 "Concordance analysis of microbial genomes" *Nucleic Acids Res.* 26:4482-4486.)

## 20 Data Curation And Analysis

Exact N-terminal and C-terminal translational start sites of genes were identified by pairwise similarity searches, multiple sequence alignments. Ribosome binding sites, terminators, nearby genes, operons were identified.

25

The resulting list of conserved genes was used as a basis for selecting and screening bacterial gene sequences that are essential for cell viability. This Concordance system was designed to permit high throughput use of the conserved gene sequences contained on the list. A set of Knockout PCR primers were generated, based on the list of  
30 conserved genes, for the purpose of use in the gene disruption procedure described below. The PCR primers were designed to amplify a central 300-500 bp region of the *ceg* (to prevent generation of a functional copy of the *ceg* gene following integration),

ordered electronically, the primers were placed in a 96-well format, and used in the gene disruption procedure as described below.

## EXAMPLE 2

5

The following provides a description of the procedure to generate recombinant vectors of pEVP-3 having inserts of candidate *ceg* nucleotide sequences. The Knockout primers generated by the method described in Example 1 above were used to generate DNA fragments comprising candidate *ceg* sequences.

10

### Genomic PCR Knockout Target Fragment Generation

96-well plate format were set up (36  $\mu$ l H<sub>2</sub>O, 5  $\mu$ l 10 $\times$  Vent<sup>TM</sup> buffer, 1  $\mu$ l gene specific, knockout forward primer (0.5  $\mu$ g/ $\mu$ l), 1  $\mu$ l gene specific knockout reverse primer (0.5  
15  $\mu$ g/ $\mu$ l), 0.5  $\mu$ l Vent<sup>TM</sup> DNA polymerase (2000 U/ml New England Biolabs, Beverly, MA), 1.5  $\mu$ l each dNTPs (10mM; 6.0  $\mu$ l total), 0.5  $\mu$ l *S. pneumoniae* chromosomal DNA (0.5  $\mu$ g/ $\mu$ l), 50  $\mu$ l total volume/reaction):

The nucleotide sequences of the forward and reverse knockout primer pairs were  
20 generated from the nucleotide sequence information obtained from the Genomic Therapeutics Corporation database for *Streptococcus pneumoniae*. The primer pairs were each used in a PCR reaction to generate a unique internal (e.g., central region) fragment of the candidate gene targeted for knockout.

25 The PCR program was set in the PCR machine (Initial 95 °C - 5 minutes; 30 Cycles of: 95 °C - 1 minute, 58 °C - 1 minute, 72 °C - 30 seconds; Final, 72 °C - 10 minutes, 4 °C – hold indefinitely). 5  $\mu$ l of each reaction was run on an 0.8% agarose gel after purifying fragment over PCR purification kit (Qiagen) to visualize the fragments then ligation reactions were performed.

30

Ligation Reactions proceeded (set up in 96-well plate format (10.0 µl genomic PCR fragment (generated from step 2 above), 1.0 µl pEPV-3 SmaI-cut vector (1: 10 dilution of vector DNA at 50-100 ng/µl), 1.5 µl 10× ligation buffer (New England Biolabs™), 1.0 µl T4 DNA Ligase (New England Biolabs™ 400,000 U/ml), 1.5 µl ddH<sub>2</sub>O, 15.0 µl total reaction volume).

Reactions were allowed to incubate in 96-well plate at 14 °C overnight in the PCR machine. Transformations into *E. coli* for in vivo amplification were proceeded the following day.

10

The nucleotide sequences of the forward and reverse primer pairs used for the polarity test were generated in a similar manner, from the nucleotide sequence information obtained from the Genomic Therapeutics Corporation database for *Streptococcus pneumoniae*. The primer pairs were each used in a PCR reaction to generate a unique fragment of the candidate gene targeted for the polarity test. The fragment generated for the polarity test included the entire *ceg* coding sequence region but lacking the expression regulatory sequences.

Transformation into *E. coli* (strain LE392):

20

The next day, 3 µl of above ligation mix was used per transformation reaction plus 50 µl LE392 competent cells. Reactions were set up in 96-well plate format; incubated on ice for 30 minutes; heat-shocked at 42° C for 90 seconds; and incubated on ice 2 minutes; 100 µl SOC media (Gibco BRL) was added; then incubated at 37° C on platform shaker for 1 hour; plated on LB/chloramphenicol (13.0 µg/ml) agar plates for constructs overnight at 37° C with plates inverted and proceeded with colony PCR to confirm constructs. The universal primers flanking the insert site in pEVP-3 were used for PCR amplification.

30 The colony PCR involved the following. 96-well plate format was set up (36.5 µl H<sub>2</sub>O, 0.5 µl pEPV3 forward primer (0.25 µg/µl), 0.5 µl pEPV3 reverse primer (0.25 µg/µl), 1.5

µl each (6.0 µl total) dNTPs (10 mM), 0.5 µl Vent™ DNA polymerase, 5 µl 10× Vent™ buffer, 1 µl of a 1:50 cell dilution, 50 µl total volume).

pEPV3 forward primer: 5' CATCAAGCTTATCGATACCGTCG 3' (SEQ ID NO:437)

5 p EPV3 reverse primer: 5' CACAGTAGTTCACCACCTTTTCCC 3' (SEQ ID NO:438)

Colonies of *E. coli* LE392 were picked onto a master plate of LB + 13 µg/ml chloramphenicol (incubate throughout the day at 37° C) and then into 50 µl H<sub>2</sub>O which has been placed into a 96-well plate. 1 µl of this dilution was used in above PCR reaction  
10 (if the 96-well dilution plate is kept you will not need to prepare a master plate). Cultures for minipreps of plasmid candidates may be prepared directly from the cell dilutions.

The PCR program was run (95 °C - 5 minutes, 30 Cycles of: 95 °C - 1 minute, 58 °C - 1 minute, 72 °C - 30 seconds, 72 °C - 10 minutes, 4 °C - hold).

15

A 10 µl/ reaction was run on a 1.0 % TBE gel. A gel designed for 96 well plates and a multichannel pipettor were used to ease loading of the sample rows. The gel was run and stained with ethidium bromide. The positive clones were identified with appropriate molecular size insert(s), amplified by the flanking pEVP-3 primers.

20

#### Minipreps Of Plasmids To Identify Cells Carrying The Pevp-3 Vector With An Insert

The constructs that carried an insert were identified. The constructs having an insert were inoculated into a 5 ml LB/Cm culture, and incubated over night at 37 °C with  
25 aeration. Miniprep plasmid DNA was prepared by a standard procedure. The miniprep DNA was digested with appropriate restriction enzymes to confirm the presence of the insert (enzymes flank SmaI site in pEVP-3) (10 µl miniprep DNA, 2 µl 10 × buffer, 1 µl XbaI, 1 µl XhoI, 6 µl ddH<sub>2</sub>O, 20 µl total volume for digest).

To confirm the presence of an insert, the digest reactions were electrophoresed on an agarose gel and the gel was stained with ethidium bromide. The positive clones were used for the *S. pneumoniae* KNOCKOUTs procedure.

- 5 The confirmatory PCR reactions, using knock out-specific primers (quality control step) involved 35.5  $\mu$ l H<sub>2</sub>O, 5  $\mu$ l 10  $\times$  Vent™ buffer, 1  $\mu$ l knockout forward primer (0.5  $\mu$ g/ $\mu$ l), 1  $\mu$ l knockout reverse primer (0.5  $\mu$ g/ $\mu$ l), 0.5  $\mu$ l Vent™ (6.0  $\mu$ l total) DNA Polymerase (2000 U/ml), 1.5  $\mu$ l each dNTPs (10mM, 6.0  $\mu$ l total), 1.0  $\mu$ l miniprep DNA from test clone, 50  $\mu$ l total reaction volume. The PCR program was as follows: 95 °C for 5  
10 minutes, 30 Cycles of: 95 °C for 1 minute, 60 °C for 1 minute, 72 °C for 30 seconds, 72 °C for 10 minutes, hold at 4 °C. The presence of the correct-sized insert was confirmed by agarose gel electrophoresis and ethidium bromide staining. The confirmed clones were used for the *S. pneumoniae* gene KNOCKOUT procedure. Glycerol stocks were made of all positive *E. coli* LE392 constructs and frozen at - 80 degrees C.

15

### EXAMPLE 3

- The following provides a description of the high throughput gene disruption procedure used in *S. pneumoniae* strain (e.g., gene knockout procedure). The candidate *ceg*  
20 fragments that were generated by the method described in Example 2 were used in the gene disruption procedure in order to identify *ceg* nucleotide sequences that are required for cell viability.

- Reactions were set up in a 1.5 ml eppendorf tubes or 96 well plate (1  $\mu$ g total of miniprep  
25 pEVP-3 + insert DNA (usually 10  $\mu$ l of Qiagen miniprep DNA); then 200  $\mu$ l of *S. pneumoniae* (strain Rx-1) competent cells diluted 1:10 in competence media was added (1 ml of competence media = 980  $\mu$ l Todd Hewitt (Difco Laboratories) with 0.5% yeast extract, 20  $\mu$ l 10% BSA, 1  $\mu$ l 10 % CaCl<sub>2</sub>, and 0.5  $\mu$ l (200  $\mu$ g/ml) Csp-1 competence peptide).

30



Controls were run with each KNOCKOUT experiment and involved 1 µg pEPV3 *Lyt A* construct = positive control (non-essential), or 1 µg pEPV3 *Fts Z* construct = negative control (essential). Then the 96 well plates and controls were incubated at 37 °C for 2.5 to 3 hours in 37 °C room without shaking. The 200 µl of the samples were plated on  
5 Todd Hewitt agar plates with 0.5% yeast extract and 2 µg/ml chloramphenicol.

The samples were incubate over night at 37 °C in 5% CO<sub>2</sub> incubator. Control plates were checked for presence of colonies (pEVP-3::*lytA*) and no growth (pEVP-3::ftsZ). Plates were examined for growth (ca. 70-150 colonies) designating nonessentials and zero  
10 colonies designating essential genes.

The polarity test was performed in a similar manner, using the polarity fragments described in Example 3.

15

#### EXAMPLE 4

The following provides a description of the autolysin procedure used to determine that the non-essential control samples of *S pneumoniae* contain a disrupted *lytA* gene.

20

##### Phenotypic Autolysin Test

The culture plates containing transformants carrying the *lytA* control vector were flooded  
25 with 0.1% deoxycholate in H<sub>2</sub>O. The plates were observed after 5-10 minutes. Plates with "ghosts" indicated intact *lytA* gene, or plates without "ghosts" indicated a disrupted *lytA* gene. The "ghost" phenomenon is due to detergent triggered autolysis of the cells, causing a gradual fading of the colonies.

30 The detergent treatment triggers the autolysin in *lytA* intact cells; it cannot trigger the autolysin (*lytA* gene product) in *lytA* disrupted cells. Colonies with intact *lytA* "ghost" in 5-10 minutes due to massive pneumococcal cell lysis.

## EXAMPLE 5

The following provides a description of the procedure used to express the CEG proteins  
5 (e.g., designated CFE proteins) in *E. coli* cells.

### CEG Protein Production

Full-length *ceg* gene were inserted into pET-21 expression vector using the *E. coli* BL21  
10  $\lambda$ DE3 expression system using the following method:

For each *ceg*, custom primers were used to insert N- and C- termini into vectors such that  
the 5' end (N-terminus of the CEG) is positioned properly for expression behind the T7  
promoter and optimally placed with regard to the pET ribosome binding site. The pET  
15 vectors contain an *NdeI* site which allows positioning of ATG start site in the vector. In  
cases where the *ceg* sequence contains an internal *NdeI* site, blunt ligation of the *ceg* PCR  
fragment into the vector is accomplished via Klenow fill-in of the *NdeI* site. In many  
cases, primers were also designed such that the *ceg* 3' (C-terminus of the expressed  
20 protein) will contain an in-frame extension of 6X-histidine residues, encoded in the  
vector sequence of pET-21. The individual *cegs* were PCR amplified via custom  
designed primers as described above. Both *ceg* PCR and vector DNA were digested with  
appropriate restriction enzymes. The full-length *ceg* were ligated into the pET  
expression vector. The ligation mixture was transformed into competent *E. coli* BL21  
25  $\lambda$ DE3 cells and selected for transformants on LB agar with 50  $\mu$ g/ml ampicillin. Positive  
insert bearing clones were screened via minipreps of the plasmids and size analysis on  
0.8% agarose gels, with detection by ethidium bromide staining, as above.

### Protein Production

30 The proper reading frame of each *ceg* inserted into pET-21 is verified by DNA  
sequencing.

A small (2-5 ml) test culture of *E. coli* BL21  $\lambda$ DE3 with the insert-bearing plasmid is tested for protein expression by IPTG induction of the expression vector for 1-2 hours. The expression is verified by SDS-Polyacrylamide Gel Electrophoresis analysis of a whole cell extract (SDS extract of 0.5-1 ml of cells treated at 100 °C for 5 minutes) to determine whether the protein is over-expressed and migrates at the correct predicted molecular weight.

The protein is overproduced and purified via the following method. A large scale (500-1000ml) culture of *E. coli* is grown to early logarithmic phase in broth (e.g., LB broth) and protein expression induced for 2 hours with IPTG (isopropyl-D-thiogalactoside). The cells are harvested by centrifugation (8000 X G; 15 minutes) and the cell pellets resuspended in 20 ml. of buffer. The cells are lysed by sonication, and the supernatant fluid centrifuged at low speed (5000 X G, 15 min.) to remove unbroken cells. The supernatant fluid, containing the over-expressed protein is subjected to Ni-NTA affinity column chromatography (Quiagen, Inc., Chatsworth, CA). The 6X-histidine residues linked at the C-terminal end of the CEG proteins permit rapid protein purification via selective binding to a Ni-NTA resin column. The protein-bound Ni-NTA resin was to remove contaminants, and the bound proteins subsequently eluted with imidazole and recovered. It is possible to upscale this procedure to larger volumes for higher yields of proteins.

#### EXAMPLE 6

The following provides a description of the methods used to purify all 2CEG polypeptides (e.g., 2CFE polypeptides #19-117; SEQ ID NOS:349-436) having a histidine tag at their C-terminal ends. The 2CEG polypeptides having the his-tags were produced by the methods described in Example 5, *supra*. As an example, results of purification of 2CFE 75 polypeptide are presented.

### Production Of The CFE Polypeptides

The BL21λDE3 cells harboring recombinant pET-21 vectors carrying a 2CFE nucleotide sequence (SEQ ID NOS:244-331) were cultured in LB broth containing ampicillin.

- 5 When the A<sub>600</sub> reached approximately 0.6, protein production was induced by adding 1.0 mM of IPTG, the cells were cultured for an additional 2 hours. The cell pellet was collected by centrifugation, and the collected cell pellet was sonicated in Solution A (50 mM NaPO<sub>4</sub>; 300 mM NaCl, pH 8.0). The sonicated cells were centrifuged at 10,000 RPM to remove the debris.

10

### Purification Of The CFE Polypeptide

The supernatant was diluted with Solution A, loaded onto a Ni-NTA column (Quiagen) equilibrated with Solution A; the column bed size was 2.5 x 25 cm, and the flow rate was approximately 3.0 ml/minute. The 2CFE protein was eluted using a linear gradient of imidazole, using 0-250 mM in 450 ml, flow rate approximately 3.0 ml/minute. The eluted samples were collected as 22 ml fractions per tube and the eluted samples were monitored using spectrophotometry. The amount of protein in the eluted fractions was estimated using the Bradford method (Bradford, M. M., 1976 *Anal. Biochem.* 72:248) and

15 the samples were run on an SDS-PAGE gel (Novex EC6008) (Figure 3 A). Fractions were selected for pooling based on the results of the SDS-PAGE gel. The pooled fractions were concentrated using a 10,000 MW Centricon (Amicon) to approximately 5 ml.

- 25 The 2CFE 75 polypeptide, a precipitate formed and was redissolved upon increasing the sample volume and removing the imidazole by repeated concentration in 50 mM Tris, 100 mM NaCl, pH 7.5. Varying amounts of the 2CFE 75 polypeptide were diluted in either 20 mM Tris, 20 mM KCl, pH 7.5 or 20 mM Tris, 20 mM MgCl<sub>2</sub>, pH 7.5 at concentrations of 12, 24, or 36 ug/ml. The diluted samples were electrophoresed on an
- 30 SDS-PAGE gel under non-reducing conditions (Figure 3 B). The results of Figure 3 B suggests that 2CFE 75 forms a multimer.

**EXAMPLE 7**

The following provides a description of the methods used to purify CEG polypeptides that lack a histidine tag (e.g., 2CFE polypeptides #1-17; SEQ ID NOS:332-348). As an example, the results of purification of CFE 3 polypeptide are presented.

Purification of the CFE 3 Polypeptide

The 2CFE 3 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 3 (SEQ ID NO:334) polypeptide lacks a C-terminal histidine tag. The 2CFE 3 polypeptide was purified using a 2-column procedure. The 2CFE 3 polypeptide preparation was eluted from a 26/10 Q Sepharose column (Pharmacia) using a 0-1.0 M NaCl gradient, 2 ml/minute flow rate, and the gradient size was 1 liter. Then the 2CFE 3 polypeptide was eluted from a hydroxyapatite Bio-gel column (Bio-Rad) using a 5-200 mM potassium phosphate (pH 8.0) gradient, the flow rate was 0.3 ml/minute, and the gradient size was 300 ml. A sample of the 2CFE 3 preparation was run on a polyacrylamide gel (Figure 4).

**EXAMPLE 8**

The following provides a description of the size exclusion chromatography methods used to estimate the molecular weight and determine whether the CEG polypeptides oligomerize. The CFE polypeptide may oligomerize to form monomers, dimers, tetramers, hexameric rings, or other oligomeric forms.

Size exclusion chromatography was performed on all isolated 2CFE polypeptides #s 1-117 (e.g., SEQ ID NOS:332-436). This method was performed using various types of columns, depending on the particular 2CFE polypeptide tested.

The Biosil SEC-125 HPLC Gel Filtration column (BioRad Laboratories, Inc) was used, for example, to characterize CFE 8. The mobile phase was 0.2 M  $\text{KH}_2\text{PO}_4$ , 0.9% NaCl pH 6.8.

- 5 The Phenomenex 600 x 7.5 mm Biosep SECS 3000 column was used, for example to characterize 2CFE 21 and 39. The mobile phase for size exclusion was 50 mM  $\text{Na}_2\text{HPO}_4$ , pH 7.0 and 150 mM NaCl run at 1 ml/minute in a Gilson HPLC system, with protein detection at 280 nm.

## 10 EXAMPLE 9

The following provides a description of the computer-aided methods used to search for similarities between the amino acid sequences of the CEG polypeptides and sequences available through public and proprietary databases. In many cases, the function of the CEG polypeptides was suggested by the results of the similarity searches. The function of some of these CEG polypeptides has been confirmed by performing additional analyses. Table V provides a list of the suggested and confirmed functions of CEG polypeptides designated CFEs #1-117.

- 20 The putative function of the CFE polypeptides were determined using computer-aided bioinformatic approaches, including distant homologies, motif searching, or predictions based on statistical rules. For example, the distant homology approach involved pairwise or multiple sequence alignments, employing tools such as FASTA, and Psi-BLAST. The motif searching approach involved using sophisticated hidden Markov models. The approach based upon predictions of statistical rules involved prediction of transmembrane regions, coiled-coil, and other structural motifs. These approaches have been reviewed in *Computational Methods In Molecular Biology* 1998, eds. Salxber, S.L., Searls, D.B. Searls, and Kasif, S., Elsevier, and in *Bioinformatics: A Practical Guide To The Analysis Of Genes And Proteins* 1998 eds Baxevanis, A. D. and Francis Ouellete, B.F., Wiley-Interscience.

30

Global sequence similarity searches were performed using the amino acid sequences of all the conserved essential gene sequences (e.g., CFEs 1-117; SEQ ID NOS:114-226) to search against a non-redundant protein database using the BLAST2 algorithm (Altschul S.F., et al., 1997 *Nucleic Acids Res.* 25(17):3389-3402). In a similar search, similar  
5 sequences were identified in the Concordance database using the "Neighbor" function (Brucoleri R. E., Dougherty T.J., Davison D.B. 1998 *Nucleic Acids Res.* 26(19):4482-4486). To determine if the predicted amino acid sequences were full length and in the proper reading frame, BLAST-type searching and CLUSTAL multiple sequence alignments (Higgins D.G., et al., 1996 *Methods Enzymol.* 266:383-402) were used.  
10 Local sequence similarity searches were performed, by searching for Prosite (Hofmann K., et al., 1999 *Nucleic Acids Res.* 27(1):215-219) and Pfam motifs (Bateman A., et al., 2000 *Nucleic Acids Res.* 28(1):263-266). Additionally, the amino acid sequences of the CFEs were analyzed by performing protein threading analyses using the ProCeryon fold recognition program (Sippl, et al., 1992 *Proteins* 13:258-271; Sippl, J. 1993 *J. Comp.*  
15 *Aided Mol. Design* 7:473-501; www.proceryon.com) and Geneformatics.

In bacteria, many operons include genes encoding different proteins that catalyze discrete steps of a common biochemical pathway. Therefore, the operon structures in *S. pneumoniae* was compared with that in other bacteria in order to predict the function of  
20 CFE polypeptides.

Additionally, analysis of bacterial metabolic pathways were performed using Pathway Tools from DoubleTwist, based on the EcoCyc system (Karp P.D., et al., 1999 *Nucleic Acids Res.* 1999 27(1):55-58). This analysis was used to predict which CFEs mediate  
25 various steps of the pathways.

When the sequence identity between a CFE polypeptide and the annotated database (e.g., SwissProt, Genbank) was low (e.g., sequence identity less than about 30%), a Protein Threading (e.g., fold recognition) method was used to predict similarities in the folded  
30 protein structure of CFE polypeptides in the absence of a high level of sequence similarity with proteins in the databases (review by Teichmann, et al., 1999 *Current Opinion in*

*Structural Biology* 9:390-399). The Protein Threading method predicts the compatibility of a query sequence (e.g., CFE polypeptide sequences) with each of the folds in a library of known protein structures. The library of known protein structures as developed, maintained, and updated throughout the search process.

5

A list of potential structural folds, onto which each query was compatible, was generated for all CFE polypeptides (e.g., SEQ ID NOS:114-226). The fold assignments for each query were used to generate pairwise sequence alignments. The pairwise sequence alignments were used to generate protein models of the query polypeptide (e.g., CFE polypeptides).

10

The pairwise sequence alignments were also used to compare the position of critical residues of the structural template with the query polypeptide. The list of critical residues was generated by using multiple sequence alignments derived from a structural classification of proteins to generate a conservation profile which provided sequence-specific positions conserved across a homologous family of protein folds. Comparative modeling was used to search the model of the query polypeptide for the critical residues and determine whether the structural and functional motifs are conserved in the query protein. Conservation of structural and functional motifs permitted assignment of putative structure and function to a query polypeptide sequence.

20

The Protein Threading method was used to search for putative folded structure and function for all CFE polypeptides (SEQ ID NOS:114-226). The CFE polypeptides having significant sequence identity (e.g., more than 30%) to known proteins were assigned putative functions with a high level of confidence.

25

#### **EXAMPLE 10**

The following provides a description of the methods used to characterize purified, CFE 101 polypeptide. The 2CFE, 101 polypeptide mediates the conversion of pantothenate to 4' phosphopantothenate, and is predicted to be a pantothenate kinase.

30



### Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the amino acid sequence of the CFE 101 polypeptide (SEQ ID NO:210) is 42% similar to the amino acid sequence of the coaA protein of *E. coli*. Thus, CFE 101 may be a pantothenate kinase, which mediates the conversion of pantothenate to 4' phosphopantothenate (Figure 5).

### Circular Dichroism and Circular Dichroism Thermal Melt Analysis

Circular dichroism and circular dichroism melt methods were used to determine the folded structure of the expressed and isolated 2CFE polypeptides. For example, this method was used to characterize the folded structure of isolated 2CFE 101 (SEQ ID NO:421).

The starting concentration of the 2CFE 101 polypeptide was such that OD<sub>205</sub> was approximately 1.5, and the OD<sub>280</sub> was approximately 0.05 (e.g., 0.05 to 0.1 mg/ml). The starting concentration of 2CFE 101 was approximately 344  $\mu$ M in 50% glycerol, 50 mM Tris, 100 mM NaCl, 5 mM MgCl<sub>2</sub>, 0.5 mM EDTA, at pH 7.5. The polypeptide was diluted to a final concentration of 7  $\mu$ M, as determined by absorbance at A<sub>280</sub>, in 20 mM Na-phosphate, 100 mM KCl, at pH 7.0. The circular dichroism analysis was performed using quartz cuvettes, the instrumentation was from JASCO (Model J-720), the readings were performed at 25 degrees C (Figure 6 A). The band width was 1 nm, the sensitivity was 20 mdeg, the response was 0.25 seconds, the scan speed was 50 nm/minute, and the step was 0.5. The circular dichroism thermal melt analysis was performed at a range of between 0 and 100 degrees C (Figure 6 B). Additionally, the circular dichroism was performed comparing monomer and aggregate pools of 2CFE 101.

### Size Exclusion Analyses

Size exclusion chromatography methods were performed using the Biosil SEC column, as described in Example 8 *supra*. The results suggest that the 2CFE 101 polypeptide forms monomer (40,200 Da) and oligomers (194,000 Da). The specific activity of the monomer and oligomeric forms of 2CFE 101 were determined, as described below.

### Biochemical Assays

The biochemical assays of the 2CFE 101 polypeptide was based on the PK/LDH coupled enzyme assays described by Vallari, D. S., et al. (1987 *J. Biol. Chem.* 262:2468-2471) and Song, W. -J., et al., (1994 *J. Biol. Chem.* 269:27051-27058).

Briefly, the assay was performed as follows. The reaction included: 885  $\mu$ l of 0.1 M Tris-HCl (pH 7.6), 25  $\mu$ l NADH (14.1 mM), 20  $\mu$ l ATP (10.7 mM), 50  $\mu$ l phospho-enol-pyruvate (56 mM), 5  $\mu$ l LDH/PK (lactose dehydrogenase/PK; Sigma, catalog # P-0294, 60 U/ ml PK, 1050 U/ml LDH), 5  $\mu$ l of the 2CFE 101 polypeptide (9 mg/ml in 50 mM Tris-HCl, pH 7.5, 100 mM NaCl which was diluted to 4.5 mg/ml in 50% glycerol). The reaction was started by adding 10  $\mu$ l pantothenate (100 mM; Sigma, catalog # P2250). The production of ADP in the reaction was monitored by measuring the absorbance at 340 nm. The results in Figure 8 show that the 2CFE 101 polypeptide mediates ADP production in the presence of pantothenate and ATP. The  $K_m$  of pantothenate ( $n=4$ ) was 144 ( $\pm 16.5$ )  $\mu$ M, the  $V_{max}$  of the 2CFE 101 polypeptide ( $n=4$ ) was 2.04 ( $\pm 0.25$ )  $\mu$ M  $\text{min}^{-1}$   $\text{mg}^{-1}$ . The monomer form has a specific activity of approximately 1.7  $\mu$ M  $\text{min}^{-1}$   $\text{mg}^{-1}$ . The oligomeric form has a specific activity of 0.26  $\mu$ M  $\text{min}^{-1}$   $\text{mg}^{-1}$ .

Alternatively, the 2CFE 101 polypeptide can be tested in an assay that monitors the conversion of pantothenate to 4'-phosphopantothenate. The same reaction described above can be used, except  $^{14}\text{C}$ -labeled pantothenate is used. The reaction can be monitored by measuring the amount of  $^{14}\text{C}$ -labeled 4'-phosphopantothenate produced.

**EXAMPLE 11**

The following provides a description of the methods used to characterize purified, CFE 39 and CFE 21 polypeptides, carrying a C-terminal histidine 6-tag. The methods include  
5 helicase reactions, in which synthetic Holliday Junction templates are resolved into duplex structures. In one method, helicase reaction was monitored using radiolabeled templates. In another method, the helicase assay was adapted for use in a high throughput assay employing fluorescence labeled templates.

**10    Computer-Aided Comparison**

The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 39 polypeptide (SEQ ID NO: 148) is an RuvA homologue. The comparison also suggests that CFE 21 (SEQ ID NO:132) is an RuvB homologue.

15

Previous studies by Parsons and others have shown that RuvA and RuvB proteins, in *E. coli*, promote branch migration or movement of Holliday Junctions during genetic recombination and DNA repair (Parsons, C. A., et al., 1992 *Proc. Natl., Acad. Sci. USA* 89:5452-5456; Tsaneva, I. R., et al., 1993 *Proc. Natl., Acad. Sci. USA* 90:1315-1319;  
20 Muller, B., et al., 1993 *J. Biol. Chem.* 268:17179-17184; Mitchell, A. H. and S. C. West 1996 *J. Biol. Chem.* 271:19497-19502; Parsons, C. A. and S. C. West 1993 *J. Molec. Biol.* 232:397-405; Tsaneva, I. R., et al., 1992 *Molec. Gen. Genet.* 235:1-10; Mitchell, A. H. and S. C. West 1994 *J. Molec. Biol.* 1994 243:208-215).

**25    Size Exclusion Chromatography**

Size exclusion chromatography was performed on 2CFE 39 (SEQ ID NO:366) and 2CFE 21 (SEQ ID NO:350) using the Phenomenex 600 x 7.5 mm Biosep SECS 3000 column, as described in Example 8 *supra*. Protein standards (BioRad) were used to calibrate the  
30 column, including thyroglobulin (670,000 Da), gamma globulin (158,000 Da), ovalbumin (44,00 Da), myoglobin (17,00 Da), and B-12 (1350 Da).

The results indicate that 2CFE 39 (RuvA) forms tetramers and 2CFE 21 (RuvB) forms a hexameric ring structure. Selected eluted samples were electrophoresed on a polyacrylamide gel (Novagen) (Figure 9).

5

#### The Holliday Junction Analysis Using Radiolabeled Templates

The Holliday Junction analysis was performed using radiolabeled, synthetic, asymmetrical, Holliday Junction templates, as described in Hiom, K. and S. C. West  
10 1995 *Cell* 80:787-793. The Holliday Junction templates were produced by annealing together four separate, single-stranded, oligonucleotide strands to form four-stranded structures (e.g., the Holliday Junction template). The Holliday Junction templates were reacted with the 2CFE 39 and 2CFE 21 polypeptides, in a helicase reaction, to test their ability to generate two duplex structures.

15

#### Producing the Synthetic Holliday Junction Templates

The asymmetrical Holliday Junction templates were produced by annealing the following oligonucleotide sequences:

20

Oligonucleotide strand 1:

5'-CCAGTGATCACATACGCTTTGCTAGGACATCTTGATATCAGCCACGTT  
CACCCGCCTACCAAGTGCCACGTTGTATGCCACGTTGACC-3' (SEQ ID NO:438)

25 Oligonucleotide strand 2:

5'-GGGTCAACGTGGGCATACAACGTGGCACTGGTAGGCGGGTGAACGTGGG  
CTGATATCAAGATGTCCATCTGTCCGTTTCATCTATGACGT-3' (SEQ ID NO:439)

Oligonucleotide strand 3:

30 5'-AACGTCATAGATGAACGGACAGATCATGGTGCTTTTAAAGTCTAGAGAC  
TATCGAGCATTAGTACCAGTATCGAATCCGTCTTGTC-3' (SEQ ID NO:440)

Oligonucleotide strand 4:

5'-TTTGACAAGACGGATTCGATACTGGTACTAATGCTCGATAGTCTCTAGAC  
TTTAAAAGCACCATGTAGCAAAGCGTATGTGATCACTG-3' (SEQ ID NO:441)

5

Oligonucleotide strand 3 was labeled at the 5' end using approximately 300 ng of oligonucleotide strand 3, 1  $\mu$ l 10x Phosphate Buffer, 5  $\mu$ l  $^{32}$ P ATP, 1  $\mu$ l T4 polynucleotide kinase (Gibco-BRL)), in a 10  $\mu$ l volume, and the reaction was performed at 37 degrees C for 30 minutes. The reaction was loaded onto a G50 column to remove the  
10 unincorporated radiolabel. The final concentration of the radiolabeled oligonucleotide strand 3 was approximately 15 ng per  $\mu$ l.

Approximately equimolar amounts of the four oligonucleotide strands were annealed (e.g., hybridized). The annealing reaction included: 5  $\mu$ l Annealing Buffer (200 mM  
15 Tris-Cl pH 8.0, 100 mM MgCl<sub>2</sub>, 1 M NaCl, 10 mM DTT); 450 ng of radiolabeled oligonucleotide strand 3; and 1000 ng each of oligonucleotide strands 1, 2, and 4; in 50  $\mu$ l total reaction volume. The control annealing reaction included: 5  $\mu$ l Annealing Buffer, 60 ng radiolabeled oligonucleotide strand 3; 1000 ng oligonucleotide strand 4; in 50  $\mu$ l total reaction volume. Annealing was performed at 95 degrees C for 5 minutes, 65  
20 degrees C for 30 minutes, 42 degrees C for 30 minutes, and room temperature (e.g., between about 23 to 27 degrees C) for 30 minutes to generate the synthetic Holliday Junction templates. The synthetic Holliday Junction templates were gel or column-purified to remove the duplex and non-annealed products. As a control, oligonucleotide strands 3 and 4 were annealed to form duplex structures. The synthetic Holliday Junction  
25 templates and duplex structures were stored at -20 degrees C.

#### CFE 39 and CFE 21: The Helicase Reaction Using Radiolabeled Templates

The helicase reaction was performed to determine whether 2CFE 39 and 2CFE 21  
30 resolved the synthetic Holliday Junction templates into duplex structures. The helicase reaction was performed as follows. A 50  $\mu$ l total reaction volume included: 25  $\mu$ l of 2x

Reaction Buffer (50 mM Tris-Cl pH8.0, 30 mM MgCl<sub>2</sub>, 2 mM ATP); 1 µl synthetic Holliday Junction template (36 ng); 2 µl 2CFE 39 (1 µM); and 2 µl 2CFE 21 (1 µM). The reaction was incubated at 37 degrees for 30 minutes. The reaction was stopped by adding 5 µl Stop Buffer (100 mM Tris-Cl pH 7.5, 5 mg/ml Proteinase-K, 5% SDS). The  
5 stopped reaction was returned to 37 degrees C for 5 minutes. The helicase reaction was loaded onto and run on a non-denaturing, 12% PAGE, Tris-glycine gel.

The results shown in Figure 10, lanes 6, 7 and 8, indicate that the 2CFE 39 and 2CFE 21 polypeptides resolved the synthetic Holliday Junction templates into duplex structures.

10

#### CFE 39: The Helicase Reaction

It has been previously shown that *E. coli* RuvA binds to Holliday Junction templates (Parsons, C. A., et al., 1992 *Proc. Natl. Acad. Sci. USA* 89:5452-5456). The ability of *S.*  
15 *pneumoniae* CFE 39 to bind to a Holliday Junction template can be tested by employing the helicase assay described herein. The results of the helicase assay can be monitored by performing a gel shift assay and/or capillary electrophoresis. The presence of a Holliday Junction template bound to 2CFE 39, which migrates more slowly than the Holliday Junction template alone, would indicate that *S. pneumoniae* 2CFE 39 binds to Holliday  
20 Junction templates.

#### CFE 39 and CFE 21: Holliday Junction Analysis Using Fluorescent-Labeled Templates

The helicase reaction described herein was performed using Holliday Junction templates  
25 having one oligonucleotide strand labeled with a fluorescent agent and another strand labeled with a quenching agent. The 5' fluorescent end and the 3' quenching end of the strands that make up the Holliday Junction templates are in proximity to each other, resulting in a non-fluorescent template. When the Holliday Junction templates are resolved into duplex structures, the fluorescent and quench ends are not in proximity to  
30 each other, resulting in fluorescence.

The Holliday Junction templates used to perform this experiment comprised the following: the 5' end of oligonucleotide strand 1 was labeled with a fluorescein (e.g., the fluorescent agent), and the 3' end of oligonucleotide strand 4 was labeled with DABCYL (e.g., the quenching agent). The oligonucleotide strand 1 labeled with fluorescein and the  
5 oligonucleotide strand 4 labeled with DABCYL were custom synthesized (Gibco-BRL Life Technologies, Inc.).

The fluorescein and DABCYL labeled oligonucleotides were annealed in a reaction, as described above, to generate synthetic Holliday Junction templates. The helicase reaction  
10 was performed as described above. The results of the helicase reaction were monitored by measuring the unquenching of the Holliday Junction templates with time (Figure 11).

The helicase assay using Holliday Junction templates labeled with fluorescent-quenching agents can be adapted for use in high throughput analyses to test 2CFE 39, 2CFE 21, and  
15 other polypeptides for their ability to resolve the templates into duplex structures.

## EXAMPLE 12

The following provides a description of the methods used to characterize purified, CFE 8  
20 polypeptide, which lacks a histidine tag. The CFE 8 is a putative DNA single-stranded binding protein.

### Computer-Aided Comparison

25 The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 8 polypeptide (SEQ ID NO:121) may be a single strand binding protein homologue, such as SSB.

### Size Exclusion Chromatography

The 2CFE 8 polypeptide (SEQ ID NO:339) was characterized by size exclusion chromatography, using the Biosil SEC-125 HPLC Gel Filtration column as described in Example 8 *supra*. The chromatogram showed one peak corresponding to a molecular weight of approximately 89 kDa. Based on the nucleotide sequence, the predicted molecular weight of 2CFE 8 is 17,351 Da. In non-denaturing conditions, 2CFE 8 forms a multimer.

### 10 Binding Reaction

The 2CFE 8 polypeptide was reacted with a single-stranded oligonucleotide A. Briefly, the binding reaction included: 50  $\mu$ M of 2CFE 8 polypeptide, 50  $\mu$ M oligo strand A, 20 mM Tris/20 mM KCl pH 7.5. The binding reaction was performed at 37 degrees C, for 2 hours.

Oligonucleotide strand A:

5'-TTAGGGCCCGGGCTATCTTACAATCTCGTT-3' (SEQ ID NO:442)

### 20 Capillary Electrophoresis

The results of the binding reaction was monitored by capillary electrophoresis, following the methods described in "Handbook of Capillary Electrophoresis" 2<sup>nd</sup> Edition, 1997, ed. J. Landers.

25

Separation was performed using an uncoated capillary tube (360  $\mu$ m o.d., 50  $\mu$ m i.d., with a 50 cm effective separation length; Watrex International, Inc., Pittsford, NY) and 50 mM borate pH 9.3 as the mobile phase, at 25 kVolts, 20 minutes separation time.

30 The results indicate that 2CFE 8 alone elutes as a sharp peak, indicating little adsorption to the uncoated capillary wall (Figure 12 A). The shape of the peak and peak retention



time changed with 2CFE 8 in the presence of all oligonucleotides tested (Figure 12 B). As a negative control, MurB polypeptide (Pucci, M. J., L. F. Discotto, and T. J. Dougherty 1992 "Cloning and Identification of the *Escherichia coli* murB DNA sequence, which encodes UDP-N-acetylenolpyruvoylglucosamine reductase" *J. Bacteriol.* 174:1690-1693) was reacted with the same oligonucleotides. MurB reacted with or without the oligonucleotides showed no change in peak shape or retention time.

After capillary electrophoresis analyses, the 2CFE8 alone and 2CFE plus oligonucleotide samples were run on native polyacrylamide gels to determine whether the polypeptide was intact. The results indicate that in all cases, 2CFE 8 was intact and had not degraded with time or storage.

#### Mobility Shift Assays

The ability of 2CFE 8 polypeptide to bind oligonucleotide strand A was tested in a mobility shift assay.

The results indicate that 2CFE 8 binds single stranded oligonucleotides (Figure 13 A and B). In Figure 13 A, the gel was stained with ethidium bromide. The unbound oligonucleotides appear near the bottom of the gel, while the bound oligonucleotides appear near the middle. The same gel was stained with Coomassie (Figure 13 B), revealing that 2CFE 8 polypeptide bound to the oligonucleotide migrated further than unbound 2CFE 8, due to the change in charge carried by the oligonucleotide. Various ratios of 2CFE8:oligo were tested. The optimal binding ratio was 2:1.

#### The Effect of MgCl<sub>2</sub>

The 2CFE 8 polypeptide precipitated in the presence of 5 mM MgCl<sub>2</sub>. The precipitation was reversible by the addition of 1  $\mu$ M of the oligonucleotides tested. The observation indicates specific binding between 2CFE 8 polypeptide and the oligonucleotides tested.

### Scintillation Proximity Assay

Scintillation proximity assay (SPA) methods can be used in a high throughput screening procedure to monitor, for example, a binding reaction. SPA utilizes beads (Amersham) which are coated on the surface with a particular compound or molecule. For example, the SPA bead may be coated with avidin to facilitate binding with any molecule having a biotin tag.

The binding reaction of the 2CFE 8 polypeptide and the oligonucleotide strand A can be monitored using SPA beads and a scintillation counter. The beads can be coated with avidin, the 2CFE 8 polypeptide can be tagged with biotin, and the oligonucleotide strand A can be radiolabeled.

### **EXAMPLE 13**

The following provides a description of the methods used to characterize purified, 2CFE 3 (SEQ ID NO:334) and 2CFE 86 (SEQ ID NO:409) polypeptides.

The 2CFE 3 polypeptide catalyzes the conversion of D-glucosamine-6-phosphate to D-glucosamine-1-phosphate, indicating that 2CFE 3 mediates amino-sugar biosynthesis through the N-acetyl glucosamine pathway (Figure 14).

The 2CFE 86 polypeptide catalyzes the conversion of D-glucosamine-1-phosphate to N-acetylglucosamine-1-phosphate, and the conversion of N-acetylglucosamine-1-phosphate to UDP-N-acetylglucosamine-1-phosphate, which indicates that 2CFE 86 also mediates amino-sugar biosynthesis through the N-acetyl glucosamine pathway (Figure 14).

### Computer-Aided Comparisons Of CFE 3

The computer-aided comparison, as described in Example 9 *supra*, suggested that the CFE 3 polypeptide (SEQ ID NO:116) is a phosphoglucosamine mutase, such as GlmM.

### Purification of the CFE 3 Polypeptide

The 2CFE 3 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 3 polypeptide lacks a C-terminal histidine tag.

- 5 The 2CFE 3 polypeptide was purified using a 2-column procedure. The 2CFE 3 polypeptide preparation was eluted from a 26/10 Q Sepharose column (Pharmacia) using a 0-1.0 M NaCl gradient, 2 ml/minute flow rate, and the gradient size was 1 liter. Then the 2CFE 3 polypeptide was eluted from a hydroxyapatite Bio-gel column (Bio-Rad) using a 5-200 mM potassium phosphate (pH 8.0) gradient, the flow rate was 0.3  
10 ml/minute, and the gradient size was 300 ml. A sample of the 2CFE 3 preparation was electrophoresed on an SDS polyacrylamide gel (Figure 4).

### Affinity Capillary Electrophoresis of CFE 3

- 15 Affinity capillary electrophoresis methods were used to determine whether the 2CFE 3 polypeptide binds to various glucose derivatives. Binding was performed under equilibrium conditions, in which the sugars were dissolved in the running buffer and reacts with 2CFE 3 during separation in the column. The affinity capillary electrophoresis method used to analyze 2CFE 3 follows the methods described in  
20 "Handbook of Capillary Electrophoresis" 2<sup>nd</sup> Edition, 1997, ed. J. Landers.

- Briefly, 2CFE 3 polypeptide was reacted with increasing amounts of various glucose derivatives (e.g., substrate) at 25, 30 and 37 degrees C. The glucose derivatives included UDP-glucose, glucose-1-phosphate, glucose-6-phosphate, glucosamine-1-phosphate, and  
25 glucosamine-6-phosphate. The reaction included: 2CFE 3 polypeptide (2.0 mg/ml), separation buffer (25 mM Tris; 192 mM Glycine, pH 8.0; BupH Tris-Glycine Buffer Packs, Pierce). Separation was performed at 25 kVolts, separation time was 15 or 20 minutes.

- 30 The results shown in Figure 15 A indicate that at 25 degrees C, 2CFE 3 binds to D-glucose-1-phosphate in a dose-dependent manner, as the peak shape and/or the retention

time for 2CFE 3 changes in the presence of 100 and 500  $\mu$ M D-glucose-1-phosphate compared to unreacted 2CFE 3.

5 The results shown in Figure 15 B indicate that at 25 degrees C, 2CFE 3 binds to D-glucosamine-6-phosphate in a dose-dependent manner, as the peak shape and/or the retention time for 2CFE 3 changes in the presence of 100 and 500  $\mu$ M D-glucosamine-6-phosphate compared to unreacted 2CFE 3.

10 The results shown in Figure 15 C indicate that at 25 degrees C, the 2CFE 3 polypeptide also binds to glucose-6-phosphate.

A comparison of 2CFE 3 reacted with various glucose derivatives, at 30 degrees C, is shown in Figure 15 D. The results indicate that D-glucosamine-6-phosphate is a putative substrate for 2CFE 3, as this reaction exhibits the greatest change in peak shape and/or retention time.

#### CFE 3: Capillary Electrophoresis and Laser-Induced Fluorescence

20 In a further analysis of 2CFE 3 polypeptide, capillary electrophoresis was performed with laser-induced fluorescence in order to separate and detect interaction between the substrate (e.g., D-glucosamine-6-phosphate) and the product (e.g., D-glucosamine-1-phosphate) in a one dose, one time-point procedure.

25 The 2CFE 3 polypeptide was derivitized by reacting 10 mM FITC (fluorescein isothiocyanate dissolved in methanol; Calbiochem, San Diego, CA) with D-glucosamine-6-phosphate, at ambient temperature, in the dark, overnight. The FITC-derivatized 2CFE 3 polypeptide (2.0 mg/ml) was reacted with the substrate (D-glucosamine-6-phosphate and D-glucosamine-1-phosphate) for one hour.

30 Separation was performed using an uncoated capillary (360  $\mu$ m o.d., 50  $\mu$ m i.d., with a 50 cm effective separation length) and 50 mM borate (pH 9.3) as the mobile phase. The

argon-ion laser had an excitation wavelength of 488 nm and an emission filter of 520 nm (Beckman, Fullerton, CA). The results shown in Figure 16 indicate that 2CFE 3 binds and catalyzes the conversion of D-glucosamine-6-phosphate to D-glucosamine-1-phosphate.

5

#### Computer-Aided Comparison Of CFE 86

The comparison results, as described in Example 9 *supra*, suggested that the CFE 86 polypeptide (SEQ ID NO:195) is an acetyltransferase, such as GlmU which is a bifunctional enzyme in *E. coli*. It has been previously shown that, in *E. coli*, GlmU is a bifunctional protein having both the acetyltransferase and uridylyltransferase active sites (Mengin-Lecreulx, D. and J. van Heijennort 1994 *J. Bacteriol.* 176:5788-5795; Gehring, Al., et al., 1996 *Biochemistry* 35:579-585). The bifunctional enzyme catalyzes the conversion of D-glucosamine-1-phosphate to N-acetylglucosamine-1-phosphate (acetyltransferase), and catalyzes the conversion of N-acetylglucosamine-1-phosphate to UDP-N-acetylglucosamine-1-phosphate (uridylyltransferase). The  $K_m$  of the acetyltransferase and uridylyltransferase reactions has been previously calculated (Mengin-Lecreulx, D. and J. van Heijennort 1994 *supra*). Additionally, the crystal structure of GlmU from *E. coli* is known (Brown, K., et al., 1999 *EMBO J.* 18:4096-4107).

20

#### Purification of the CFE 86 Polypeptide

The 2CFE 86 polypeptide (SEQ ID NO:409) has a C-terminal histidine tag. The 2CFE 86 polypeptide was produced using the large scale IPTG-induced method described in Example 5, *supra*. The 2CFE 86 polypeptide was purified using the Ni-NTA affinity column method described in Example 6, *supra*. The eluted 2CFE 86 polypeptide was dialyzed against 50 mM Tris-Cl, 100 mM NaCl, 25% glycerol, pH 8.0. Samples of the purified 2CFE 86 polypeptide were electrophoresed on a polyacrylamide gel (Figure 17).

30

### Coupling CFE 3 and CFE 86 to Produce UDPAG

A biochemical assay was performed, to determine whether 2CFE 3 and 2CFE 86 convert D-glucosamine-6-phosphate to UDP-N-acetylglucosamine-1-phosphate (e.g., UDPAG).

- 5 The 2CFE 3 and 2CFE 86 polypeptides were used in a coupled reaction based on the assays described in Jolly, L. P., et al., 1999 *Eur. J. Biochem.* 262:202-210.

A time-dependent and dose-dependent assay were performed. Briefly, the assay was performed in 96-well plates, each well including 100  $\mu$ l volume. The assay included: 1  
10 mM D-glucosamine-6-phosphate (Sigma); 0.7 mM D-glucosamine-1,6-diphosphate (Sigma); 1.2 mM acetyl-Coenzyme A (Sigma); and 5 mM uridine-5'-phosphate (Sigma); 3 mM  $MgCl_2$  (Sigma); 50 mM Tris-Cl, pH 8.0 (Life Technologies). The reaction was started by adding 1  $\mu$ g of 2CFE 3; and 10  $\mu$ g of 2CFE 86. The reaction was performed at room temperature. The reaction was stopped at 0, 15, 30, and 65 minutes, by filtering out  
15 the 2CFE polypeptides.

The results of the assay was monitored by HPLC (high pressure liquid chromatography) using an Optisil 10 $\mu$  SAX column (250 x 4.6 mm), measuring at 262 nm, the mobile phase was 150 mM  $KH_2PO_4$  (pH 3.5), and 1.5 ml/minute flow rate. The results shown in  
20 Figure 18 show the time-dependent assay and indicate that HPLC detected the presence of UDPAG.

### CFE 86: The Uridyltransferase Reaction

- 25 The 2CFE 86 polypeptide was tested in a uridyltransferase reaction, in which N-acetyl-D-glucosamine-1-phosphate and UTP produce UDP-N-acetylglucosamine. The uridyltransferase reaction was monitored using a malachite green/inorganic pyrophosphatase assay (e.g., malachite green-IPPAse assay) and/or monitored using HPLC. The malachite green-IPPAse assay was used to measure orthophosphate  
30 production from digestion of the pyrophosphate liberated in the uridyltransferase reaction.

The malachite green reagent was prepared as follows. A 0.045 % solution of malachite green (Sigma; M9636) was prepared in water. A 4.2 % solution of ammonium molybdate (Mallinckrodt) was prepared in 4N HCl. The malachite green and ammonium molybdate were mixed in a 3:1 ratio, and stirred for about 20 minutes. The mixture was filtered, and stored at 4 degrees C. The inorganic pyrophosphatase (Sigma; I-2267) was diluted to 0.1 U/ $\mu$ l in 50 mM Tris/3mM MgCl<sub>2</sub> pH 8.0, and stored at 4 degrees C.

The uridylyltransferase reaction was performed in 96-well plates. The coupled reaction described herein was performed, in the presence of 2CFE 3 alone or 2CFE 3 and 2CFE 86, and included the addition of 0.5 U/well of the diluted inorganic pyrophosphate. The reaction was mixed for 5 minutes at room temperature. The reaction was stopped by the addition of 240  $\mu$ l/well of the malachite green reagent and 30  $\mu$ l/well of 34% sodium citrate, and the reaction was mixed. The results of the uridylyltransferase reaction was monitored by spectrophotometry at 660 nm.

The results of separate uridylyltransferase reactions were monitored by HPLC, using a Phenosphere-NEXT C18 column (250 x 4.6 mm). The mobile phases included A and B as follows: A) methanol/10 mM potassium phosphate pH 6.5 (0:100); and B) methanol/10 mM potassium phosphate pH 6.5 (40:60). The mobile phases were run under the following conditions: 100% mobile phase A for 5 minutes, to 100% mobile phase B in 3 minutes; and hold 100% mobile phase B for 9 minutes. The retention time for the UDPAG product is approximately 5.75 to 6.0 minutes.

The results three uridylyltransferase reactions, monitored by HPLC are summarized in Table III below.

**TABLE III**

| <u>Purified CFE 86:</u> | <u>Specific Activity<br/>(nmol/min/μg):</u> |
|-------------------------|---|
| 2CFE 86-1               | 3.1   |
| 2CFE 86-2               | 3.4   |
| 2CFE 86-3               | 3.1   |

5

The results of the uridylyltransferase reactions, monitored by HPLC or HPLC and Malachite Green IPPase assays are summarized in Table IV below.

10

**TABLE IV**

| <u>Reaction:</u>                     | <u>K<sub>m</sub> (μM):</u> | <u>Method:</u>     |
|--------------------------------------|----------------------------|--------------------|
| <u>Acetyltransferase reaction:</u>   |                            |                    |
|                                      | 94                         | HPLC               |
| Glucosamine-1-P                      | 150                        | HPLC               |
| Acetyl-coA                           |                            |                    |
| <u>Uridylyltransferase reaction:</u> |                            |                    |
| N-acetylglucosamine-1-P              | 48                         | HPLC and MG/IPPase |
| UTP                                  | 79                         | HPLC               |

**EXAMPLE 14**

15

The following provides a description of the methods used to characterize various 2CFE polypeptides, including CFE 21, 34, 35, 39, and 90. The molecular weight of these 2CFE polypeptides were analyzed by size exclusion chromatography and gel electrophoresis. The 2CFE 34, 35, and 90 polypeptides putatively mediate fatty acid biosynthesis.

20



### Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that CFE 34 (SEQ ID NO:143), CFE 35 (SEQ ID NO:144), and 90 (SEQ ID NO:199) are polypeptides which mediate a fatty acid biosynthesis pathway (Figure 19)

The comparison suggests that CFE 34 is a malonyl CoA:ACP transacylase, which catalyzes the reaction in which malonyl CoA and acyl carrier protein (ACP) are converted to malonyl-ACP and CoA. Thus, the CFE 34 polypeptide may be a homologue of *E. coli* FabD.

The comparison suggests that CFE 90 is a 3-oxoacyl-ACP synthase II (beta ketoacyl-ACP synthase II) which catalyzes the reaction in which malonyl-ACP is converted to beta aceto acetyl-ACP. Thus, the CFE 90 polypeptide may be a homologue of *E. coli* FabF.

The comparison suggests that CFE 35 is a 3-oxoacyl-ACP reductase (beta aceto acetyl ACP reductase) which catalyzes the reaction in which beta-keto-acetyl-ACP is converted to beta-hydroxy-acetyl-ACP. Thus, the CFE 35 polypeptide may be a homologue of *E. coli* FabG.

### Size Exclusion Chromatography

The estimated molecular weights of 2CFE 34 (SEQ ID NO:361), 2CFE 35 (SEQ ID NO:362), and 2CFE 90 (SEQ ID NO:413) were determined using the Biosil SEC-125 HPLC Gel Filtration column as described in Example 8, *supra*.

The results suggest that 2CFE 34 polypeptide is a monomeric protein (33,093 Da), 2CFE 35 is a trimeric protein (25,758 Da; approximately 85%), and 2CFE 90 is a dimeric protein (43,930 Da). Selected eluted samples of 2CFE 34 were electrophoresed on a polyacrylamide gel (Figure 20).

Biochemical Assay: CFE 34

The function of 2CFE 34 was determined by performing various biochemical reactions.

- 5 To determine whether 2CFE 34 catalyzes the conversion of malonyl-CoA to malonyl and CoA, the following reaction was performed.

The biochemical reaction was performed in the presence of acyl carrier protein. The reaction included the following: 10  $\mu\text{M}$   $^{14}\text{C}$  labeled malonyl-CoA, 20  $\mu\text{M}$  ACP, 30  $\mu\text{M}$  10 2CFE 34 (e.g., FabD) in 20 mM Tris-Cl, pH 8.0 and 5 mM DTT in 300  $\mu\text{l}$  volume. The reaction was performed at room temperature (e.g., approximately 24 degrees C) for 30 minutes. The reaction was terminated with the addition of 45  $\mu\text{l}$  of 0.5% TFA. The labeled reaction was injected onto a MonoQ 5/5 column on a Gilson HPLC. Detection was performed by monitoring the radioactivity of the continuous flow-through of the 15 HPLC effluent. Chromatography was performed using a buffer gradient for column elution. Buffer A included 20 mM Tris-Cl, pH 8.3. Buffer B was the same as Buffer A and included 1 M NaCl. The program was held at 90% A, 10% B for 10 minutes followed by a linear ramp to a final mix of 50% of each Buffer A and B over 10 minutes.

- 20 The substrate (e.g.,  $^{14}\text{C}$  malonyl-CoA) eluted at 9.9 minutes, the product (e.g.,  $^{14}\text{C}$  malonyl-ACP) eluted at 14.3 minutes. The results indicate that CFE 34 catalyzes the conversion of malonyl-CoA and acyl carrier protein (ACP) to malonyl-ACP and CoA.

**EXAMPLE 15**

25

The following provides a description of the methods used to characterize CFE polypeptides 40, 41, and 46.

Computer-Aided Comparison

The computer-aided comparison, as described in Example 9 *supra*, suggests that the CFE 40 polypeptide (SEQ ID NO:149) is a phosphomethylpyrimidine (HMP-P) kinase  
5 involved in thiamine biosynthesis.

The comparison, as described in Example 9 *supra*, suggests that the CFE 41 polypeptide (SEQ ID NO:150) has a GTP-binding motif and may be a protease.

10 The comparison, as described in Example 9 *supra*, suggests that the CFE 46 polypeptide (SEQ ID NO:155) has an ATP-binding motif.

Affinity Purification of CFE 41

15 The large-scale method described in Example 5 *supra* (e.g., IPTG-induced protein production) was used to prepare a sample of 2CFE 41 polypeptide (SEQ ID NO:368). The sample was affinity purified using the Ni-NTA method described in Example 6, *supra*. The eluted fractions were loaded onto and run on a 12% SDS-PAGE gel (Novex) (Figure 21).

20

Circular Dichroism and Circular Dichroism Thermal Melt Analysis

Circular dichroism and circular dichroism thermal melt methods were performed using JASCO instrumentation. The concentration of the isolated 2CFE 40 (SEQ ID NO:367)  
25 was approximately 21  $\mu$ M, in a 0.1 cm pathlength cell at 210 nm. The circular dichroism spectrum suggests that this preparation of 2CFE 40 had mixed alpha and beta secondary structure. The circular dichroism thermal melt spectrum suggests that 2CFE 40 has a  $T_m$  of approximately 67 degrees C. The 2CFE 40 polypeptide precipitates at approximately the  $T_m$ .

The concentration of the isolated 2CFE 41 (SEQ ID NO:368) was approximately 70  $\mu$ M, in a 0.02 cm pathlength cell. The circular dichroism spectrum suggests that this preparation of 2CFE 41 had mixed alpha and beta secondary structure, with a greater  
5 percentage of alpha structures. The circular dichroism thermal melt spectrum suggests that 2CFE 41 has a  $T_m$  of approximately 38 degrees C. The 2CFE 41 polypeptide precipitates at approximately the  $T_m$ .

The concentration of the isolated 2CFE 46 (SEQ ID NO:373) was approximately 23  $\mu$ M,  
10 in a 0.1 cm pathlength cell at 280 nm. The circular dichroism spectrum suggests that this preparation of 2CFE 46 had mixed alpha and beta secondary structure. The circular dichroism thermal melt spectrum suggests that 2CFE 46 is highly stable at elevated temperatures. At 90 degrees C, the 2CFE 46 polypeptide exhibited only a 27% loss in signal and the polypeptide remained soluble.

15

#### Capillary Electrophoresis

Capillary electrophoresis was performed on samples of purified 2CFE 40, 41 and 46. The electropherograms of 2CFE 40, 41, and 46 are shown in Figure 22.

20

#### **EXAMPLE 16**

The following provides a description of methods that can be used to characterize CEG polypeptides (e.g., CFE polypeptides).

25

#### Computer-Aided Compilation

Computer-aided compilation of bacterial metabolic pathways may be analyzed using Pathway Tools from Doubletwise, based on the EcoCyc system (Karp P.D., et al., 1999  
30 *Nucleic Acids Res.* 1999 27(1):55-58). This analysis may be used to predict which CFEs mediate various steps of the pathways. This information may be used in combination

with the results of a binding reaction which identifies a ligand or substrate that binds with a CFE polypeptide.

#### Identifying the Function of a CFE Polypeptide

5

The function of a CFE polypeptide may be identified by identifying a ligand or substrate which binds with the CFE polypeptide. The ligand or substrate may be identified using fractionation and affinity capillary electrophoresis methods. The following method is based upon the assumption that the bacterial cell lysate includes the ligand or substrate.

10

A bacterial host cells carrying an endogenous (e.g. native) CFE gene or carrying a recombinant vector which includes a CFE gene may be cultured so that the CFE polypeptide is produced by the cell. The cells may be ruptured in order to obtain the cell lysate. The cell lysate may be fractionated using HPLC technology. The HPLC fractions may be reacted with a CFE polypeptide in a binding reaction, and the binding reaction may be analyzed by affinity capillary electrophoresis methods. The ligand or substrate which reacts with the CFE polypeptide may be identified using mass spectrophotometry methods (in "Mass Spectrometry" 1990 eds. McCloskey, J. A., in *Methods in Enzymology* volume 193; Henion, J., et al., 1993 "Mass Spectrometric Investigations of Drug-Receptor Interactions" *Ther. Drug Monit.* 15:563-569; Loo, J. A., et al., 1999 "Application of Mass Spectrometry for Target Identification and Characterization" *Med. Res. Rev.* 19:307-319; Nguyen, D. N., et al., 1995 "Protein Mass Spectrometry: Applications to Analytical Biotechnology" *J. Chromatogr.* 705:21-45).

#### 25 **EXAMPLE 17**

The following provides a description of nuclear magnetic resonance (NMR) spectroscopy methods that were used to characterize CFE polypeptides.

30 High resolution NMR spectroscopy was applied to  $^{15}\text{N}$ -labeled,  $^{13}\text{C}/^{15}\text{N}$ -labeled,  $^2\text{H}/^{13}\text{C}/^{15}\text{N}$ -labeled, and type-specifically isotopically labeled CFE polypeptide samples

in the solution state for the following purposes: to assess various aspects of the structural state, e.g., foldedness, structural integrity; to refine a previously determined experimental structure of a close sequence homologue; to refine a homology-modeled structure; to assess the potential for a CFE polypeptide to bind small molecules; and to identify small-molecule pharmacophoric fragments that bind specifically to the CFE polypeptide

5 ("Nuclear Magnetic Resonance" 1994 eds. James, T. L. in *Methods in Enzymology* volume 239).

The NMR analysis includes screening both a compound deck of approximately 4,500 commercially available, structurally and chemically diverse compounds (the small-molecule pharmacophore deck) and a compound deck of proprietary, known, anti-microbial compounds (anti-microbial deck) against the CFE polypeptides (i.e., target polypeptides) to determine, either based upon perturbations to the chemical shifts of the amide proton and/or nitrogen resonances, as measured from a two-dimensional proton-nitrogen heteronuclear single-quantum correlation spectrum (2D screening method), or

15 based upon increases in the linewidth of the compound's proton resonance(s), as measured by a one-dimensional  $T_{1\rho}$  spin-lock difference spectrum (1D screening method), both whether a compound binds to a CFE polypeptide and, in the case of the 2D screening method, where the compound binds on the CFE polypeptide.

20

#### Isotopic Labeling of CFE Polypeptides

BL21-DE3 *E. coli* bacteria are transformed with the CFE expression vectors. Expression takes place between 20°C and 37°C in minimal media containing [ $^{15}\text{N}$ ]-ammonium sulfate as the sole nitrogen source and either glucose, [ $^2\text{H}$ ] $_{13}$ -glucose, or [ $^{13}\text{C}$ ] $_6$ -glucose as the sole carbon source. Glucose is used for preparing uniformly  $^{15}\text{N}$ -labeled and  $^2\text{H}/^{15}\text{N}$ -labeled CFE polypeptides. [ $^2\text{H}$ ] $_{13}$ -glucose is used for preparing type-specifically  $^1\text{H}/^{13}\text{C}$ -labeled, uniformly  $^{15}\text{N}$ -labeled CFE polypeptides. [ $^{13}\text{C}$ ] $_6$ -glucose is used for preparing  $^{13}\text{C}/^{15}\text{N}$ -labeled CFE polypeptides. The minimal media is prepared in 100%  $\text{H}_2\text{O}$  for

25 expressing both uniformly  $^{15}\text{N}$ -labeled and uniformly  $^{13}\text{C}/^{15}\text{N}$ -labeled CFE polypeptides;

30 the minimal media is prepared in 95%  $\text{D}_2\text{O}$  (deuterium oxide) and 5%  $\text{H}_2\text{O}$  for expressing

both type-specifically  $^1\text{H}/^{13}\text{C}$ -labeled, uniformly  $^{15}\text{N}$ -labeled and just uniformly  $^2\text{H}/^{15}\text{N}$ -labeled CFE polypeptides. In the case of type-specifically  $^1\text{H}/^{13}\text{C}$ -labeled, uniformly  $^{15}\text{N}$ -labeled CFE polypeptides, 40 mg/L of protonated and uniformly  $^{13}\text{C}/^{15}\text{N}$ -labeled isoleucine, valine and leucine amino acids are added to the minimal media.

5

### NMR Screening

Compounds in the anti-microbial deck are pre-dissolved to a target concentration of 16 mM in deuterated DMSO (dimethylsulfoxide) with each deck well containing only one  
10 compound. Compounds in the small-molecule, pharmacophore deck are pre-dissolved in deuterated dmso to a target concentration of 50 mM in groups of 8, i.e., each deck well contains 8 unique compounds with each compound at a target concentration of 50 mM.

3.5  $\mu\text{l}$  of compound is placed at the bottom of a well in a 96-well, screening plate. This  
15 well will be referred to as the compound screening well. Each compound screening well contains solution from only one deck well. 166.5  $\mu\text{l}$  of buffer is added to each compound screening well. 170  $\mu\text{l}$  of a CFE polypeptide solution, initially at a concentration ranging from 200-300  $\mu\text{M}$ , is added to each compound screening well; the contents of that well are then thoroughly mixed. The control screening well contains only 3.5  $\mu\text{l}$  of deuterated  
20 dmso. The screening plate is then centrifuged in a bucket rotor for 15 minutes at 3,500 rpm to insure that all particulate matter is at the bottom of the well.

The 2D screening method requires a single control screening well in which the compound solution consists only of deuterated DMSO. The 1D screening method requires a control  
25 screening well for each compound screening well. In the case of the 1D screening method, the control screening well is prepared identically to the compound screening well except that the 170  $\mu\text{l}$  of a CFE polypeptide solution is replaced by 170  $\mu\text{l}$  of buffer.

The screening plate is covered with aluminum foil and placed onto a rack of a Gilson  
30 liquid handler. The Gilson liquid handler, under computer control by the NMR host/data-acquisition software, is responsible for removing each sample from the screening plate,

injecting the sample into a high-resolution,  $^1\text{H}/^{15}\text{N}$  double-resonance NMR flow-probe, removing the sample from the flow-probe, and dispensing it back into the screening plate well from which the sample was originally removed. NMR data are collected on the sample while the sample resides in the NMR flow-probe. The type of NMR data  
5 collected depends upon whether the 2D or 1D screening method is being used.

#### Determining Structural Characteristics of a CFE Polypeptide

10 In assessing various aspects of the structural state of a CFE polypeptide, NMR was used to provide the following information. The proton 1D spectra and proton-nitrogen 2D correlation NMR spectra were used to assess the overall foldedness of a CFE polypeptide without actually describing in detail that folded state. Unfolded and substantially misfolded proteins produced distinct signatures in these two types of NMR spectra.

15 The chemical shift of most protein nuclei in either the set  $\{\text{H}_\text{N}, \text{H}_\alpha, \text{H}_\beta, \text{C}', \text{C}_\alpha, \text{C}_\beta, \text{N}\}$  or the set  $\{\text{H}_\text{N}, \text{C}', \text{C}_\alpha, \text{C}_\beta, \text{N}\}$  for perdeuterated (e.g.,  $^2\text{H}$ -labeled) proteins were determined by procedures well known in the art that involve collecting up to 10 triple-resonance NMR data sets. The protein secondary structure was delineated as either helical, turn or extended (e.g.,  $\beta$ -sheet) by measuring  $\Delta(\delta_{\text{C}_\alpha} - \delta_{\text{C}_\beta})$ ,  $\Delta\delta_{\text{C}'}$ , and  $\Delta\delta_{\text{H}_\alpha}$  where  $\delta$  refers to the  
20 chemical-shift value and  $\Delta$  refers to the difference between chemical-shift values measured in this protein and those measured for the same residue type in a random-coil (unstructured), tetrameric peptide.

This secondary-structure profile was generated in approximately 2-3 weeks per protein.  
25 The secondary-structure profile was used to confirm the functional identity of a protein. It was also used to refine the list of possible functional identities of folds, predicted by various computational techniques including fold recognition which is associated with a protein or polypeptide.



NMR was used to generate folds of proteins or polypeptides for which both no structure was known of a sequence homologue and no structural homologue was discernible in the PDB by fold recognition techniques.

## 5 Refining a Structural Model

Nuclear Overhauser (NOE) data were used to refine both homology-modeled structured and previously determined experimental structures of close sequence homologues. This process took approximately 2-3 weeks per structure.

10

The CFE 88 polypeptide was characterized by NMR analysis to establish its secondary structure. The NMR data was used to filter the computer-aided threading analysis. The NMR-determined secondary structure for CFE 88 suggested that CFE 88 is structurally similar to 4-aminoimidazole carboxylase.

15

The characteristics of other CFE polypeptides were analyzed by NMR methods. A computer-aided threading analysis revealed that the N-terminal domain of the protein EGA, which both binds and hydrolyzes GTP, was both structurally similar and sufficiently similar in sequence to CFE 52 to suggest that CFE 52 had a similar function.

20

The NMR data of CFE 103 suggests that this polypeptide is unfolded. Circular dichroism spectra, as a function of temperature, also indicated that CFE103 was unfolded.

The CFEs 2, 42, 43, 68 and 88 polypeptides were tested for their ability to bind potential inhibitor molecules by screening both the anti-microbial deck and the small-molecule, pharmacophore deck. CFE 34 was tested for its ability to bind potential inhibitor molecules by screening the anti-microbial deck.

25

Characterizing Small-Molecule Binding

NMR-based screening was used to measure binding against both the small-molecule, pharmacophore deck and the anti-microbial deck. Binding data from these screens  
5 allowed assessment of the propensity of a protein to bind small molecules. The binding data was also used to identify sites on the protein which are capable of binding small molecules. The binding data was also used to identify common pharmacophores among the compounds which bind.

- 10 Reverse screening refers to a process whereby known anti-microbial compounds, the microbial target of which is unknown, are screened by a general method, e.g., binding as assessed by NMR, to find a physical interaction with polypeptide targets previously determined to be essential to the bacteria (i.e., the CFEs). The reverse screening method was used to determine which CFE polypeptides bind to which compounds in the anti-  
15 microbial deck. The reverse screening method included the following. The compounds in a proprietary compound deck were screened for Minimal Inhibitory Concentration (e.g., MIC). The compounds exhibiting antimicrobial activity were designated active compounds. The CFE polypeptides were screened to determine which polypeptide bind to which active compounds. The CFE polypeptides which bound to the active  
20 compound(s) were confirmed, where possible, i.e., in cases where an in-vitro assay was possible to construct, as being inhibited in their function as a polypeptide by the active compound(s) by examination of the inhibition profile of the compound(s) against the CFE polypeptides. For additional confirmation, the effect of the compound on the microorganism harboring the CFE polypeptide was monitored (e.g., whole cell assays).  
25 The structure of the active compound was used as a basis to generate chemically-related compounds by iterative synthesis. The chemically-related compounds were tested in a screening assay for binding with CFE polypeptides. The active compounds and the chemically-related compounds of interest were the compounds which exhibited an increase in binding affinity for a CFE polypeptide and/or exhibited drug-like properties.

30

The results of the reverse screening are as follows. 127 compounds from the proprietary compound deck exhibited anti-microbial activity. 94 of these active compounds were selected based upon both lack of cytotoxicity and lack of excessive hydrophobicity. These 94 compounds were soluble to 16 mM in deuterated DMSO; these compounds  
5 were also deemed to be sufficiently soluble in aqueous buffer for both the 2D and 1D NMR screening methods.

This subset of 94 compounds was used in an NMR-based screen to determine which compound binds to which CFE polypeptide. The CFE 42 polypeptide bound two  
10 different compounds with  $K_d$ 's in the range of 0.2 to 1 mM; the CFE 43 polypeptide bound one compound with  $K_d \sim 30$ -50  $\mu$ M; the CFE 34 polypeptide bound 13 compounds, one of which inhibited the polypeptide function with  $IC_{50} < 10 \mu$ M.

The enzyme assay used to confirm the NMR results which suggested CFE 34 interaction  
15 with the compounds included the following: 10  $\mu$ M  $^{14}$ C-labeled malonyl CoA; 20  $\mu$ M ACP, 30 pM CFE 34; 20 mM Tris-Cl, pH 8.0; 5 mM DTT; in the presence of absence of 50  $\mu$ M of a compound solubilized at 40 mM in 100% DMSO and dilute 100-fold into 10% DMSO and further diluted 8-fold for a final concentration of 50  $\mu$ M in 1.25% DMSO. The reaction was performed at room temperature, the reaction was stopped with  
20 the addition of TFA. Two hundred  $\mu$ l of the reaction was injected onto a Mono Q 5/5 column. The chromatography conditions included: A) 20 mM Tris-Cl, pH 8.3; B) 20 mM Tris-Cl, pH 8.3, 1 M NaCl. Hold 10% B for 5 minutes, linear gradient from 10% B to 50%B in 10 minutes, back to 10% B in 1 minute, hold for 14 minutes to re-equilibrate. The reaction substrate ( $^{14}$ C- malonyl CoA) eluted at 9.9 minutes, the reaction product  
25 ( $^{14}$ C-malonyl ACP) eluted at 14.3 minutes.

What is claimed is:

1. An isolated nucleic acid molecule encoding a polypeptide which is (1) essential for the viability of a bacterial cell and (2) has at least any one of the functions of a  
5       pantothenate kinase, a Holliday Junction branch migration protein, a single  
      stranded DNA binding protein, a phosphoglucosamine mutase, an  
      acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase,  
      a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a  
      phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP  
10       binding protein, or a 4-aminoimidazole carboxylase.
2. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:97 or Figure 115 and wherein the polypeptide is a  
      pantothenate kinase.
- 15       3. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:35, Figure 60, SEQ ID NO:19, or Figure 44, and wherein  
      the polypeptide is a Holliday Junction branch migration protein.
- 20       4. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:8 or Figure 33 and wherein the polypeptide is a single  
      stranded DNA binding protein.
- 25       5. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:3 or Figure 28 and wherein the polypeptide is a  
      phosphoglucosamine mutase.
- 30       6. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule  
      is shown in SEQ ID NO:82 or Figure 103 and wherein the polypeptide is a  
      acetyltransferase.

7. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:82 or Figure 103 and wherein the polypeptide is a uridylyltransferase.
- 5 8. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:30 or Figure 55 and wherein the polypeptide is a malonyl CoenzymeA:ACP transacylase.
9. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:86 or Figure 107 and wherein the polypeptide is a 3-oxoacyl-ACP synthase II.
- 10 10. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:31 or Figure 56 and wherein the polypeptide is a 3-oxoacyl-ACP reductase.
- 15 11. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:36 or Figure 61 and wherein the polypeptide is a phosphomethylpyrimidine (HMP-P) kinase.
- 20 12. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:37, Figure 62, SEQ ID NO:48, or Figure 73, and wherein the polypeptide is a GTP binding protein.
- 25 13. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:42 or Figure 67 and wherein the polypeptide is a ATP binding protein.

14. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:84 or Figure 105 and wherein the polypeptide is a 4-aminoimidazole carboxylase.
- 5 15. The isolated nucleic acid molecule of claim 1, wherein the nucleic acid molecule is shown in SEQ ID NO:48 or Figure 73 and wherein the polypeptide is a GTP binding protein.
- 10 16. An isolated nucleic acid molecule encoding a polypeptide which is essential for the viability of a bacterial cell, the nucleic acid molecule comprising a sequence shown in any one of SEQ ID NOS:1-113.
- 15 17. An isolated nucleic acid molecule encoding a polypeptide which is essential for the viability of a bacterial cell, the nucleic acid molecule comprising a sequence shown in any one of Figures 26-130.
18. An isolated nucleic acid molecule encoding any one of a polypeptide designated CFE 1-117 having the amino acid sequence shown in SEQ ID NO:114-226.
- 20 19. An isolated nucleic acid molecule comprising a nucleotide sequence which is complementary to the nucleotide sequence of claim 1, 16, 17 or 18.
20. The isolated nucleic acid molecule of claim 1, 16, 17 or 18 which is DNA or RNA.
- 25 21. The isolated nucleic acid molecule of claim 20, which is labeled with a detectable marker.
- 30 22. The isolated nucleic acid molecule of claim 21, wherein the detectable marker is selected from the group consisting of a radioisotope, a fluorescent compound, a

bioluminescent compound, a chemiluminescent compound, a metal chelator and an enzyme.

23. A vector comprising the nucleotide sequence of claim 1, 16, 17, or 18.

5

24. A host-vector system comprising the vector of claim 23, in a suitable host cell.

25. The host-vector system of claim 24, wherein the suitable host cell is selected from a group consisting of a yeast cell, a plant cell, and an animal cell.

10

26. The host-vector system of claim 24, wherein the suitable host cell is selected from a group consisting of an *Escherichia* cell, a *Bacillus* cell, a *Pseudomonas* cell, a *Streptococcus* cell, and a *Streptomyces* cell.

15

27. An isolated polypeptide which is essential for the viability of a bacterial cell comprising the amino acid sequence as shown in any one of SEQ. ID NOS: 114-226.

20

28. An isolated polypeptide which is essential for the viability of a bacterial cell encoded by the isolated nucleic acid molecule of claim 1, 16, 17, or 18.

29. The isolated polypeptide of claim 27 or 28 which is a fusion polypeptide.

25

30. A method for producing a polypeptide having the amino acid sequence of any one of SEQ ID NOS: 114-226 or a polypeptide encoded by the polynucleotide sequence as shown in any one of Figures 26-130, comprising:

- a) culturing the host-vector system of claim 24 under suitable conditions so as to produce the polypeptide; and
- b) recovering the polypeptide so produced.

30

31. A polypeptide produced by the method of claim 30.

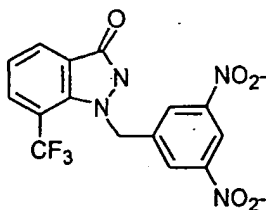
32. A ligand which binds the polypeptide of claim 27 or 28.

5 33. The ligand of claim 32 which is an antibody or an immunologically active fragment thereof.

34. The ligand of claim 33, wherein the antibody is a monoclonal antibody.

10 35. The ligand of claim 32 which is a diazalactone.

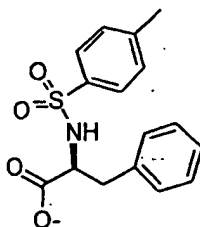
36. The ligand of claim 35, wherein the diazalactone comprises the structure:



37. The ligand of claim 32 which is a *N*-protected amino acid.

15

38. The ligand of claim 37, wherein the *N*-protected amino acid comprises the structure:

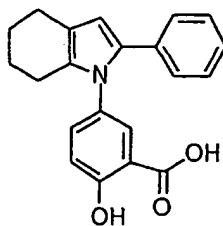


39. The ligand of claim 32 which is an azabicyclodiene.

20

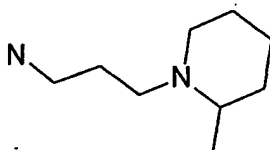


40. The ligand of claim 39, wherein the azabicyclodiene comprises the structure:



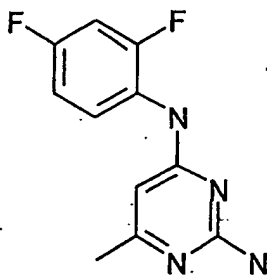
5 41. The ligand of claim 32 which is an alkaloid.

42. The ligand of claim 41, wherein the alkaloid comprises the structure:

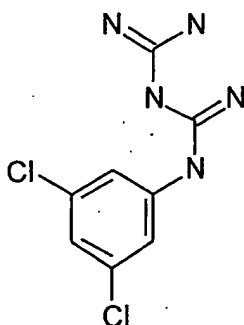


10

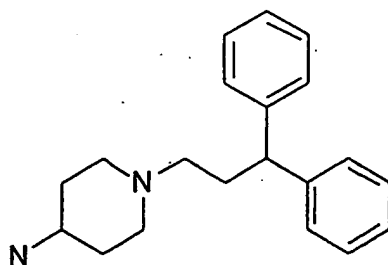
43. The ligand of claim 41, wherein the alkaloid comprises the structure:



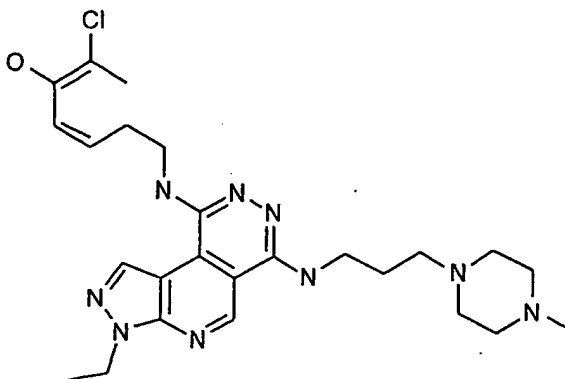
44. The ligand of claim 41, wherein the alkaloid comprises the structure:



5 45. The ligand of claim 41, wherein the alkaloid comprises the structure:



46. The ligand of claim 41, wherein the alkaloid comprises the structure:



5      47. A method for detecting the presence of the polypeptide of claim 27 or 28 in a sample, comprising contacting the sample with a ligand which binds the polypeptide and detecting the binding of the polypeptide with the ligand in the sample.

10      48. The method of claim 47, wherein the detecting comprises:

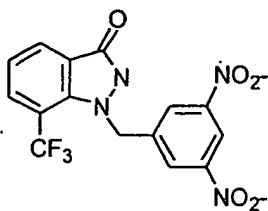
- a) contacting the sample with the ligand; and
- b) determining whether a polypeptide-ligand complex is so formed.

15      49. The method of claim 47, wherein the sample is a cell, a tissue, or a biological fluid.

50. The method of claim 47, wherein the sample is blood, serum, a swab from nose, a swab from ear, or a swab from throat.

20      51. The method of claim 47, wherein the ligand is a diazylactone.

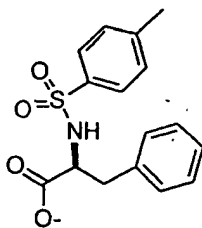
52. The method of claim 51, wherein the diazalactone comprises the structure:



53. The method of claim 47, wherein the ligand is a *N*-protected amino acid.

5

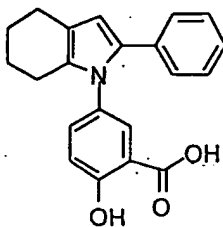
54. The method of claim 53, wherein the *N*-protected amino acid comprises the structure:



55. The method of claim 47, wherein the ligand is an azabicyclodiene.

10

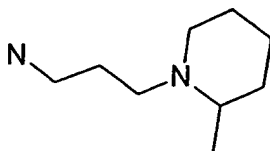
56. The method of claim 55, wherein the azabicyclodiene comprises the structure:



57. The ligand of claim 47 which is an alkaloid.

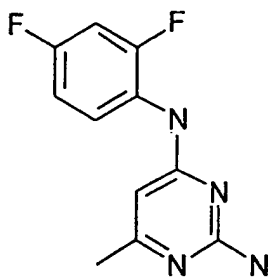
15

58. The ligand of claim 57, wherein the alkaloid comprises the structure:

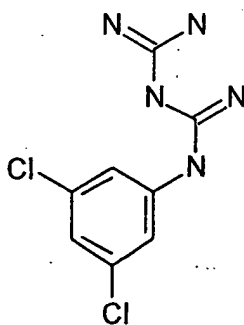


5

59. The ligand of claim 57, wherein the alkaloid comprises the structure:

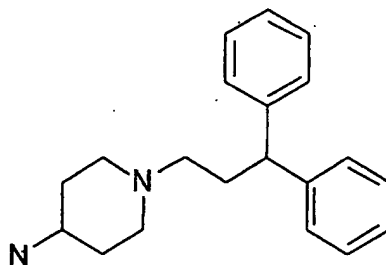


60. The ligand of claim 57, wherein the alkaloid comprises the structure:



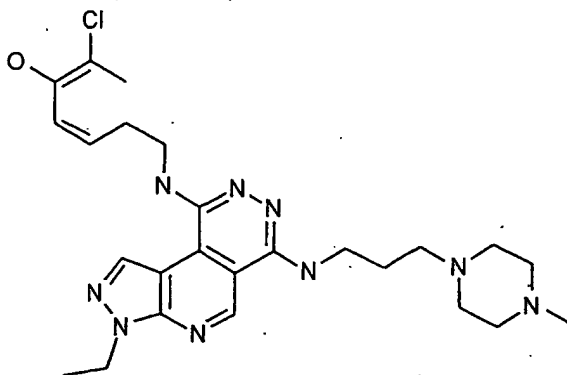
10

61. The ligand of claim 57, wherein the alkaloid comprises the structure:



5

62. The ligand of claim 57, wherein the alkaloid comprises the structure:



10

63. A method for detecting the presence of a target nucleic acid molecule as shown in any one of SEQ ID NOS:1-113 in a sample, comprising contacting the sample with the complementary nucleic acid molecule of claim 19 and detecting the binding of the target nucleic acid molecule with the complementary nucleic acid molecule in the sample.

15

64. The method of claim 63, wherein the detecting comprises:
- a) contacting the sample with the complementary nucleic acid molecule; and
  - b) determining whether a complex comprising the target nucleic acid molecule and the complementary nucleic acid molecule is so formed.
65. The method of claim 63, wherein the sample is a cell, a tissue, or a biological fluid.
66. The method of claim 63, wherein the sample is blood, serum, a swab from nose, a swab from ear, or a swab from throat.
67. A pharmaceutical composition comprising the nucleic acid molecule of claim 1, 16, 17, or 18.
68. A pharmaceutical composition comprising the polypeptide of claim 27 or 28.
69. A pharmaceutical composition comprising the ligand of claim 32.
70. A method for determining whether a genomic nucleotide sequence of interest is essential for viability of a bacterial cell, comprising
- a. integrating an exogenous nucleotide sequence into the genomic nucleotide sequence of interest, wherein the exogenous nucleotide sequence comprises a portion of an open reading frame of the genomic nucleotide sequence of interest, and
  - b. determining whether the cell having the genomic nucleotide sequence of interest so integrated is viable.
71. The method of claim 70, wherein the portion of the open reading frame comprises about 200 to 500 base pairs in length.

72. The method of claim 70, wherein the exogenous nucleotide sequence further comprises a nucleotide sequence conferring a selectable phenotype to the cell having the genome so integrated.

5

73. The method of claim 70, wherein determining comprises selecting the cell having the genome so integrated in the presence of a selection agent.

74. The method of claim 73, wherein the selection agent is chloramphenicol.

10

75. A nucleotide sequence of interest which is essential for viability of a bacterial cell isolated by the method of claim 70.

76. A bacterial cell comprising an exogenous nucleotide sequence integrated into the genomic nucleotide sequence of interest, generated by the method of claim 70.

15

77. A method for determining whether a genomic nucleotide sequence of interest resides within an operon, comprising

- a) integrating an exogenous nucleotide sequence into the genomic nucleotide sequence of interest; and
- b) determining whether the cell having the genomic nucleotide sequence of interest so integrated is viable, and wherein the exogenous nucleotide sequence lacks an expression regulatory sequence.

20

78. The method of claim 77, wherein the exogenous nucleotide sequence further comprises a nucleotide sequence conferring a selectable phenotype to the cell having the genome so integrated.

25

79. The method of claim 77, wherein determining comprises selecting the cell having the genome so integrated in the presence of a selection agent.

30



80. The method of claim 79, wherein the selection agent is chloramphenicol.

81. A method for inhibiting a function of a CEG polypeptide which is essential for viability of a bacterial cell, the method comprising contacting the CEG polypeptide with the ligand of claim 32 under suitable conditions thereby inhibiting the function of the CEG polypeptide.

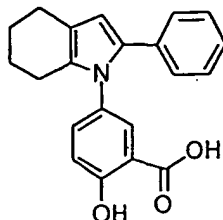
82. The method of claim 81, wherein the function of the CEG polypeptide is selected from a group consisting of a pantothenate kinase, a Holliday Junction branch migration protein, a single stranded DNA binding protein, a phosphoglucosamine mutase, an acetyltransferase, an uridylyltransferase, a malonyl CoenzymeA:ACP transacylase, a 3-oxoacyl-ACP synthase II, a 3-oxoacyl-ACP reductase, a phosphomethylpyrimidine (HMP-P) kinase, a GTP binding protein, a ATP binding protein, or a 4-aminoimidazole carboxylase.

83. The method of claim 81, wherein the CEG polypeptide is selected from a group consisting of CFE1-113.

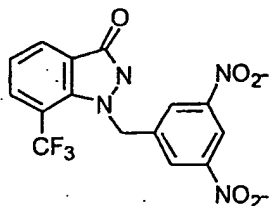
84. The method of claim 81, wherein the CEG polypeptide is 2CFE 34 shown in Figure 55.

85. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in Figure 64.

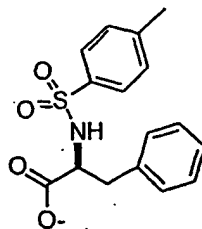
86. The method of claim 81, wherein the CEG polypeptide is 2CFE 34 shown in Figure 55 and the ligand is:



5 87. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in Figure 64 and the ligand is:



10 88. The method of claim 81, wherein the CEG polypeptide is 2CFE 43 shown in Figure 64 and the ligand is:



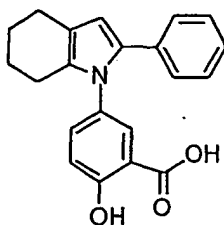
89. A method for identifying a ligand in a sample which specifically binds a CEG polypeptide, the method comprising:

- a) contacting the CEG polypeptide with the sample under suitable conditions so that a complex having the CEG polypeptide and the ligand is formed;
- b) recovering the complex so formed ; and
- c) separating the CEG polypeptide from the ligand in the complex and identifying the ligand so separated.

90. The method of claim 89, wherein the sample is a tissue or biological fluid.

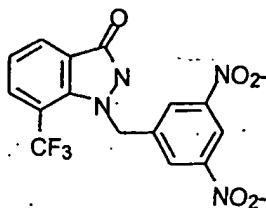
91. The method of claim 89, wherein the ligand is an azabicyclodiene.

92. The method of claim 91, wherein the azabicyclodiene comprises the structure:



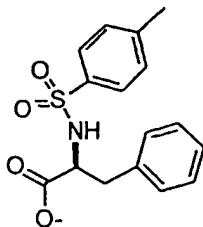
93. The method of claim 89, wherein the ligand is a diazalactone.

94. The method of claim 93, wherein the diazalactone comprises the structure:



95. The method of claim 89, wherein the ligand is a *N*-protected amino acid.

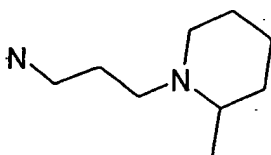
96. The method of claim 95, wherein the *N*-protected amino acid comprises the structure:



5

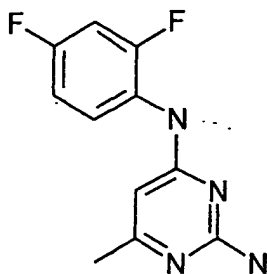
97. The method of claim 89, wherein the ligand is an alkaloid.

98. The ligand of claim 97, wherein the alkaloid comprises the structure:



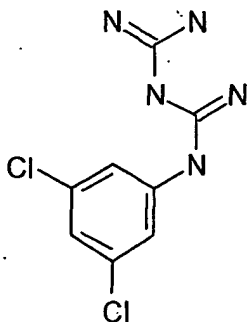
10

99. The ligand of claim 97, wherein the alkaloid comprises the structure:



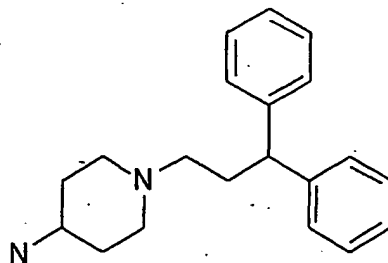
15

100. The ligand of claim 97, wherein the alkaloid comprises the structure:

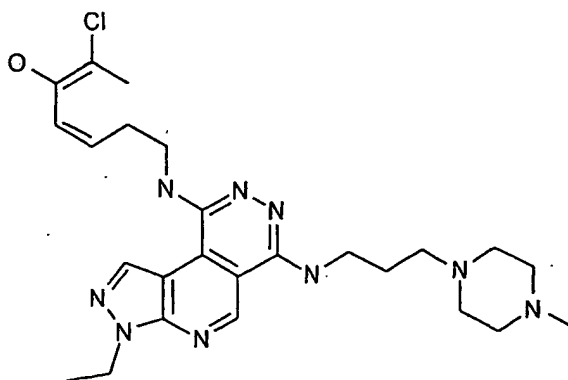


101. The ligand of claim 97, wherein the alkaloid comprises the structure:

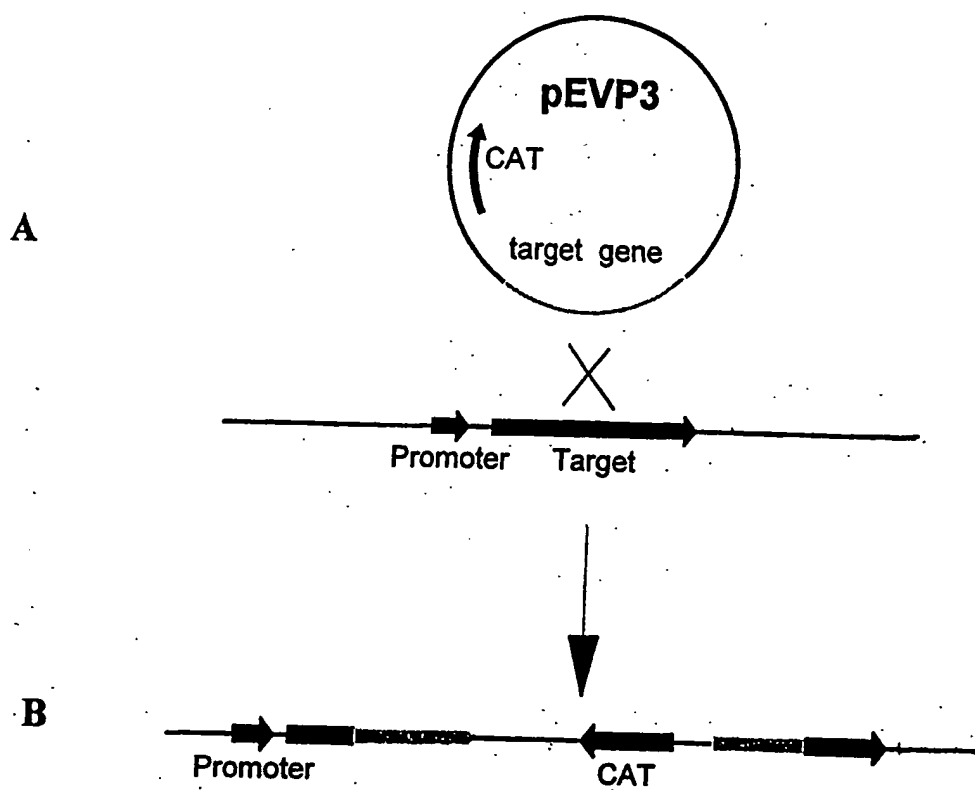
5



102. The ligand of claim 97, wherein the alkaloid comprises the structure:

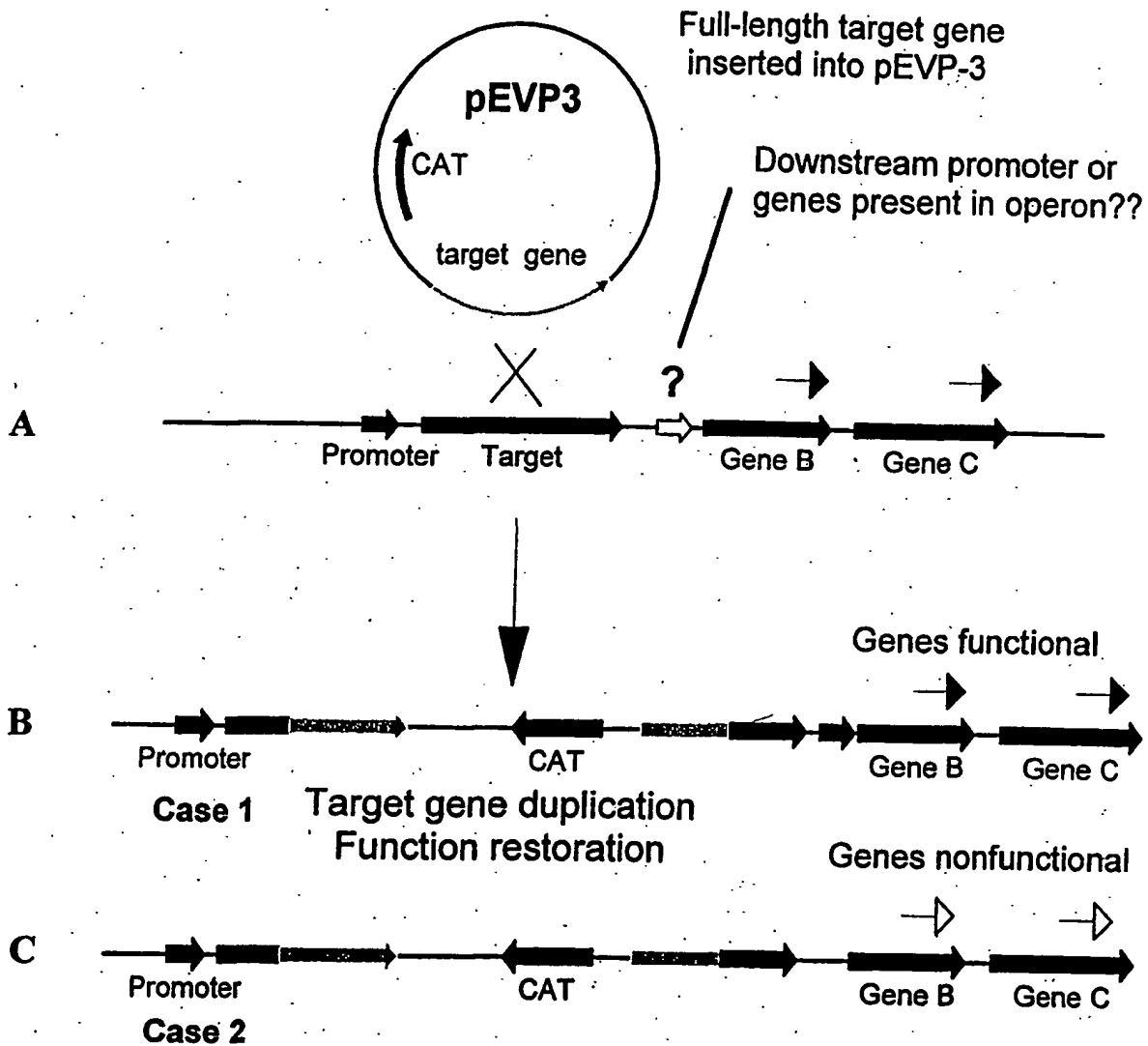


# Gene Disruption Assay



**FIGURE 1**

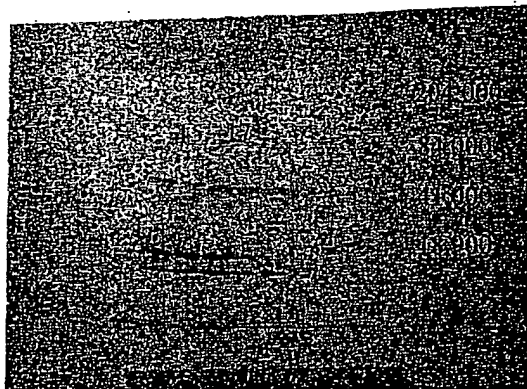
# Polarity test for Operons



**FIGURE 2**



A.



B.

204,000

12 24 36

41,000

17,000 MW proteins

FIGURE 3

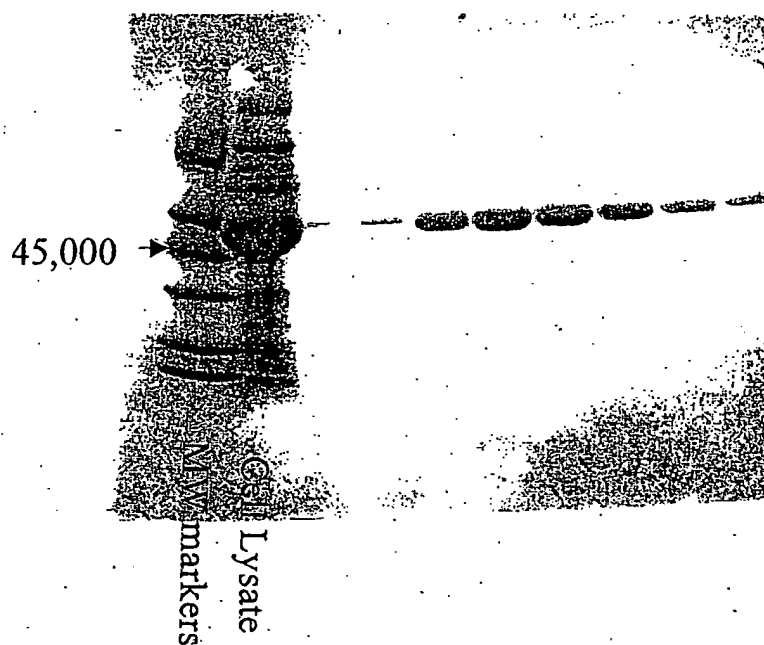


FIGURE 4

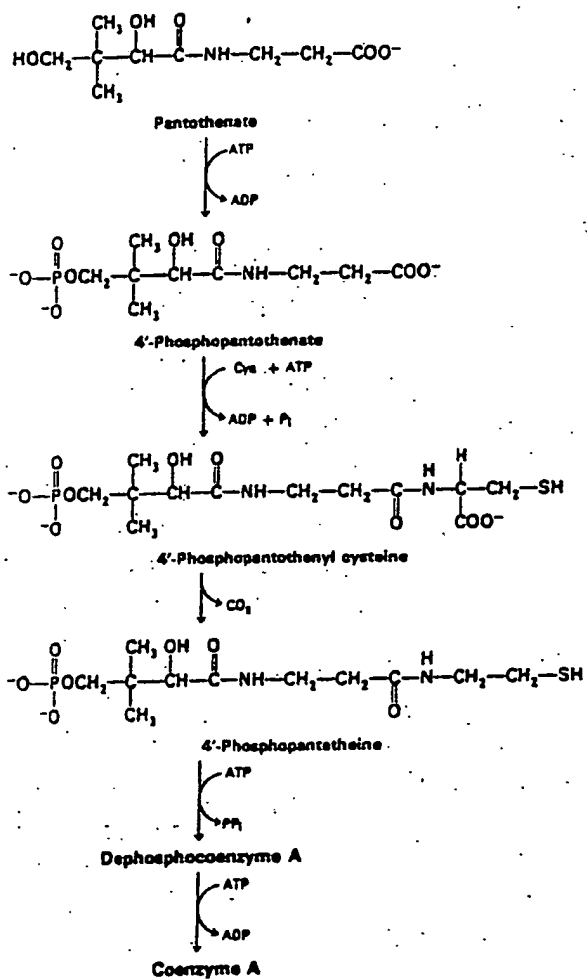
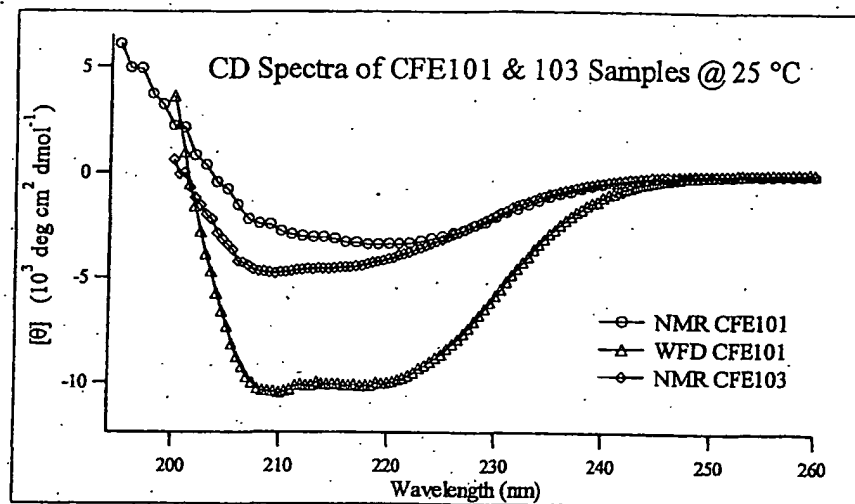


FIGURE 5

A.



B.

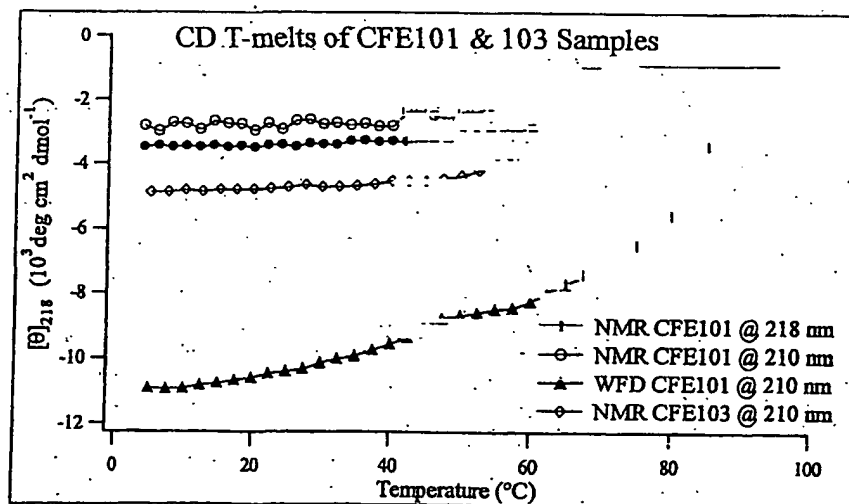
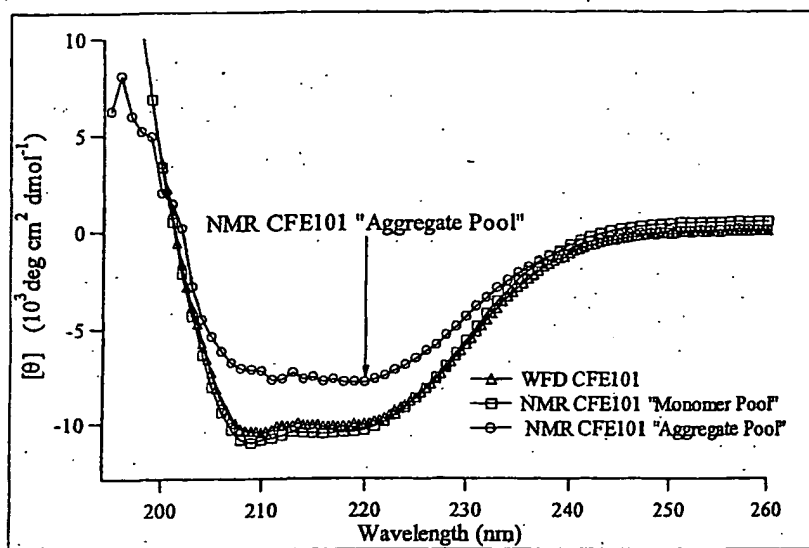


FIGURE 6

A.



B.

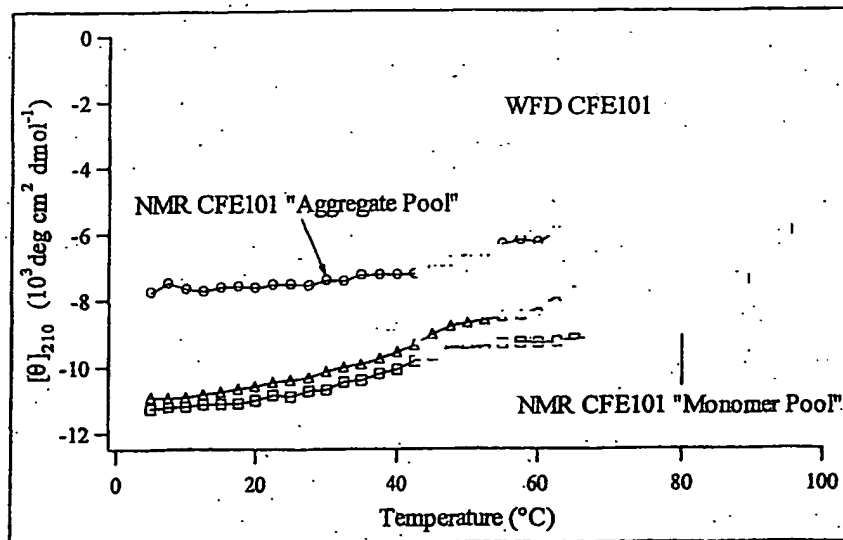


FIGURE 7

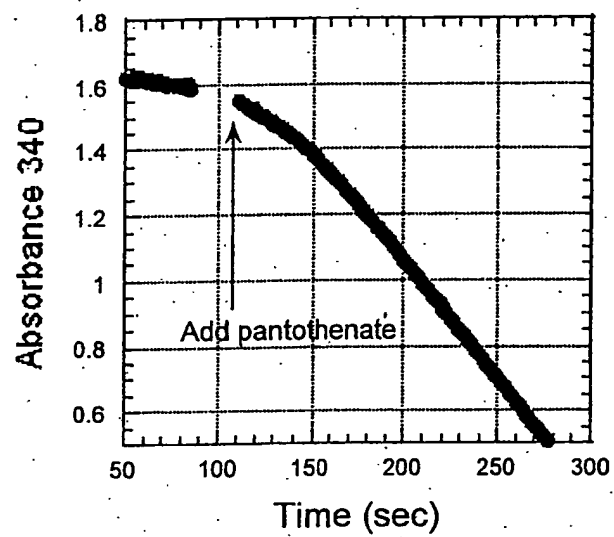


FIGURE 8

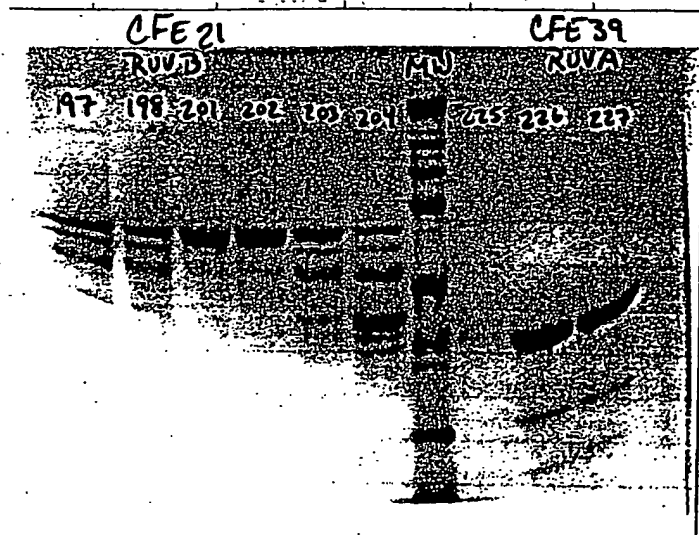


FIGURE 9

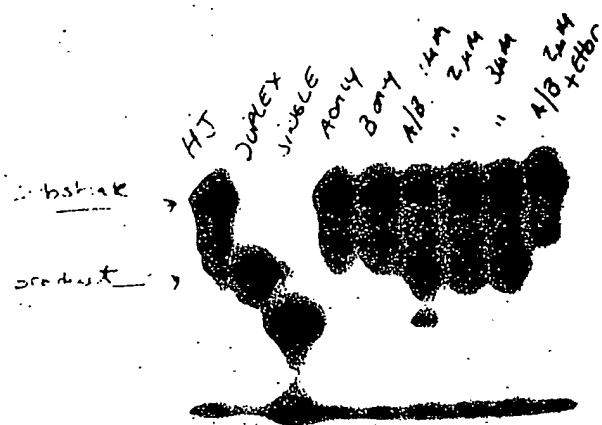


FIGURE 10



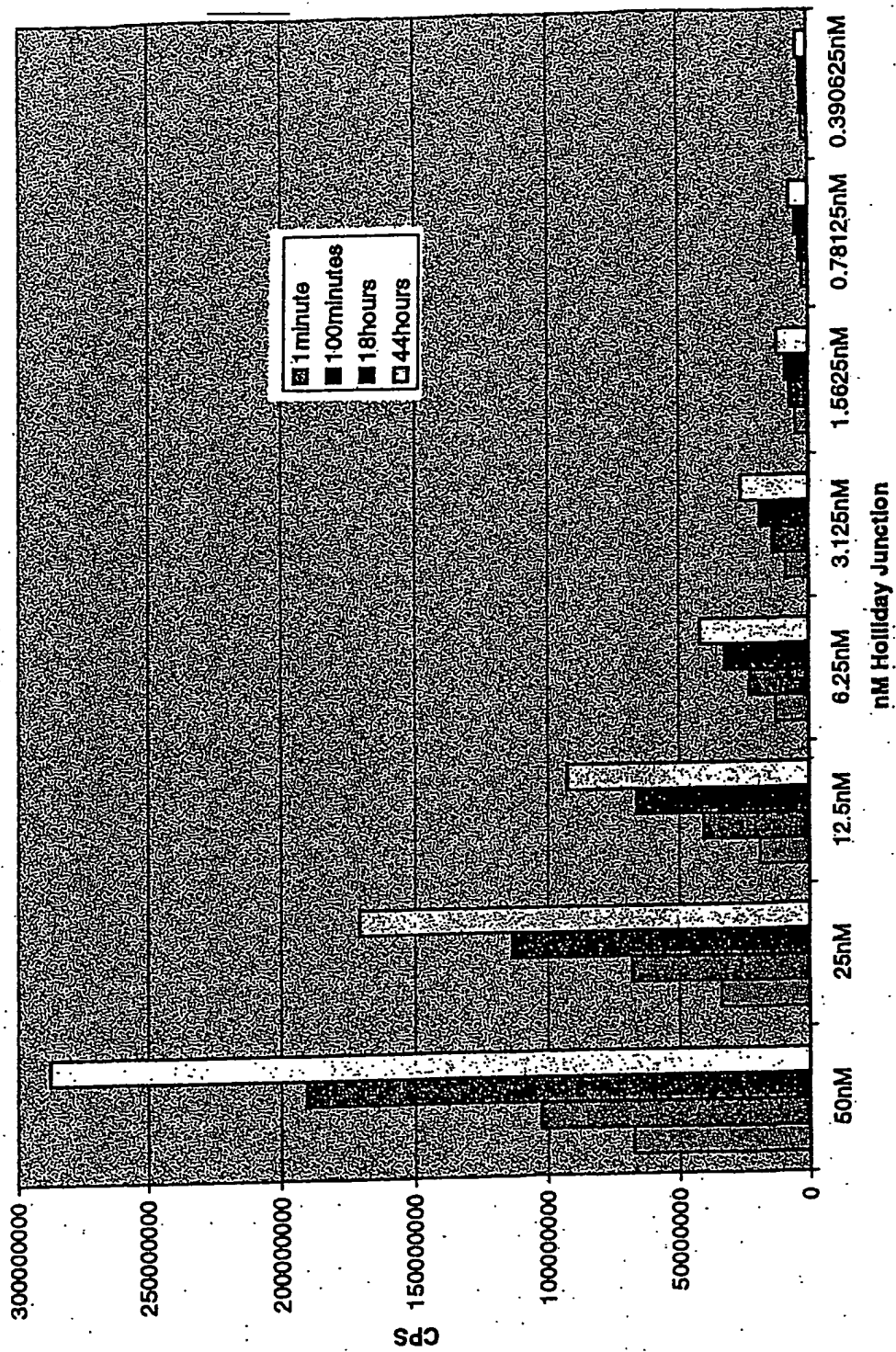


FIGURE 11

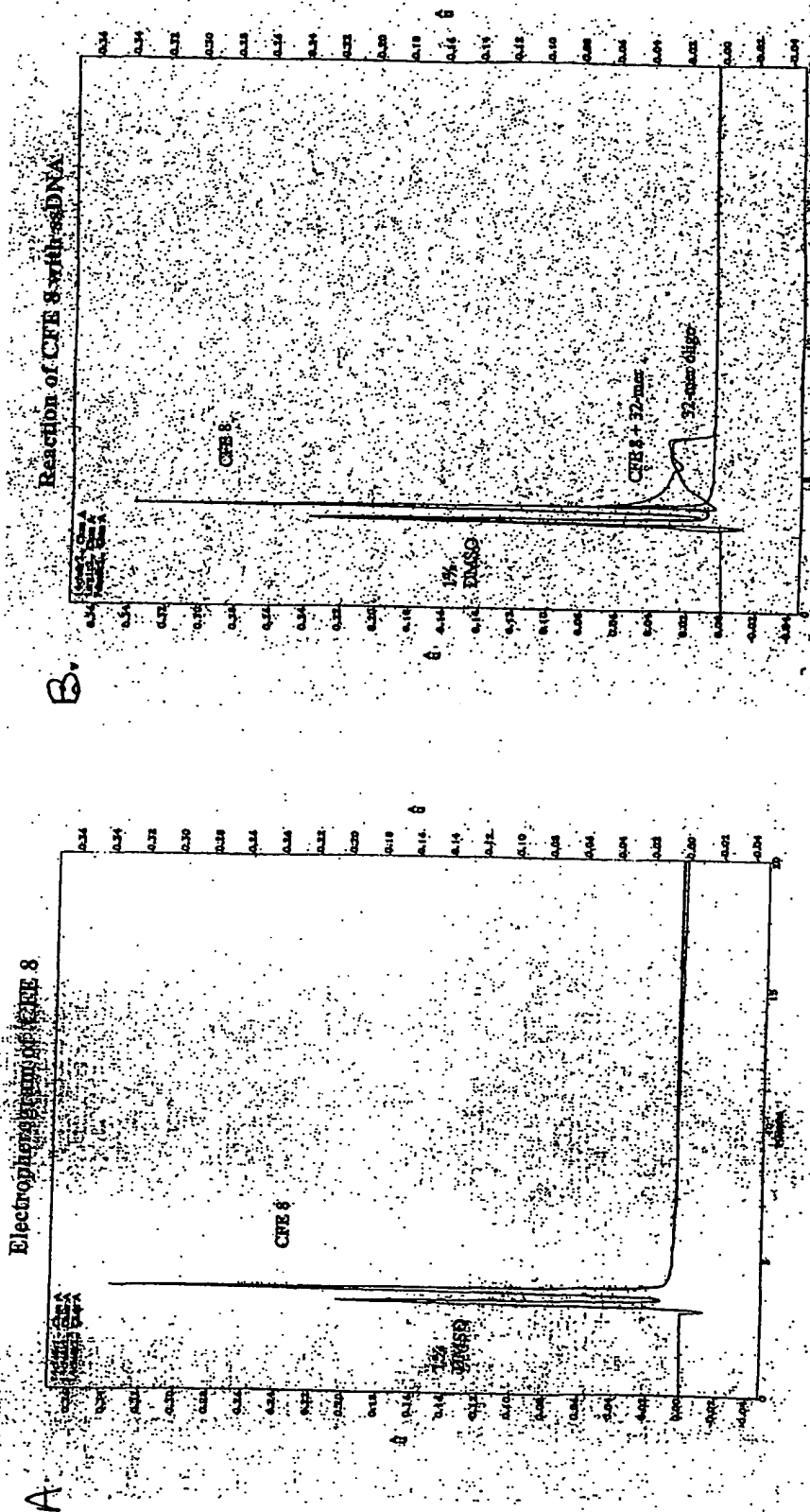


FIGURE 12

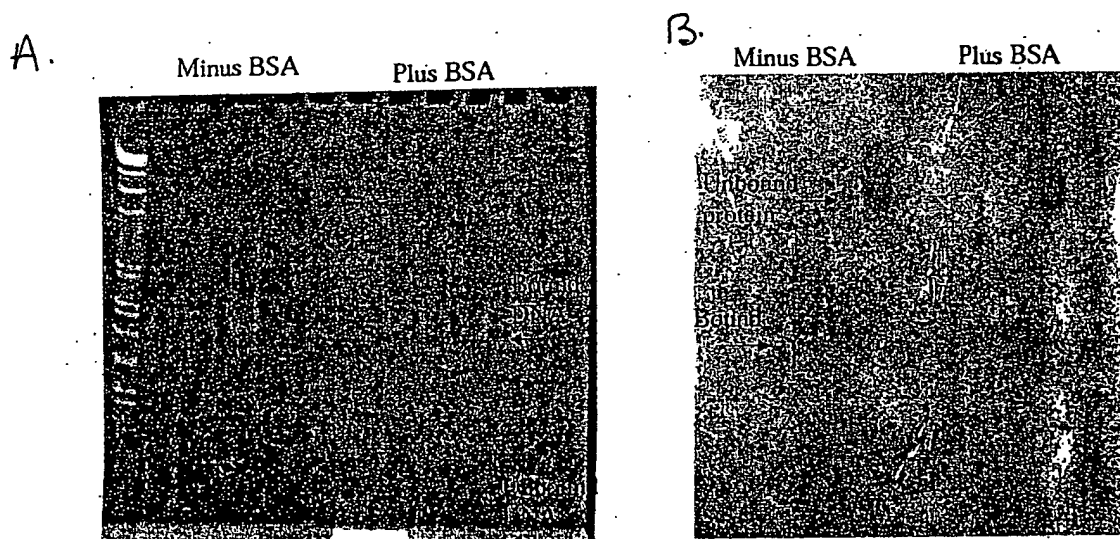


FIGURE 13

## N-Acetyl Glucosamine Pathway

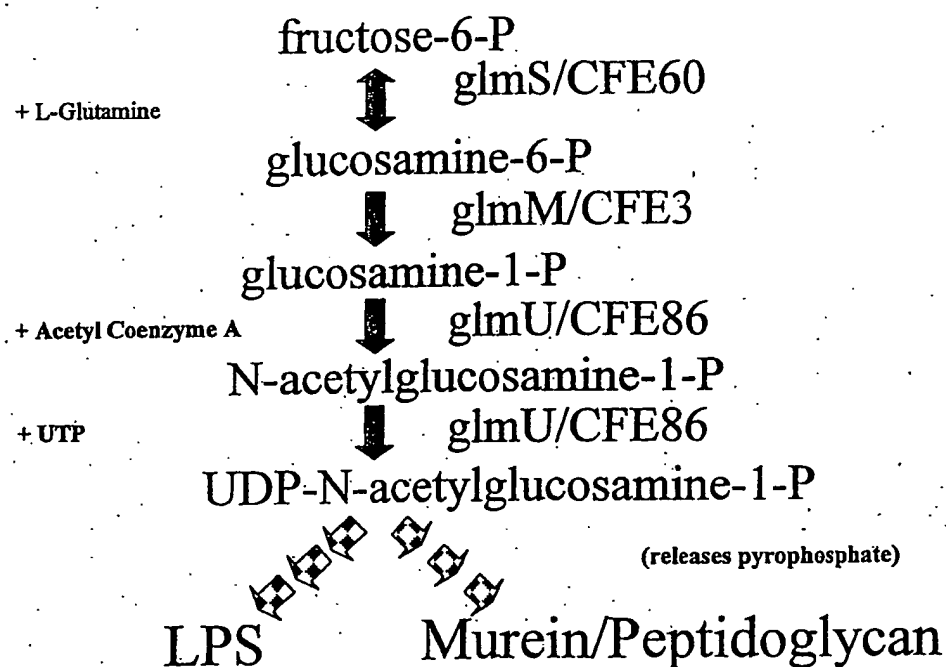


FIGURE 14

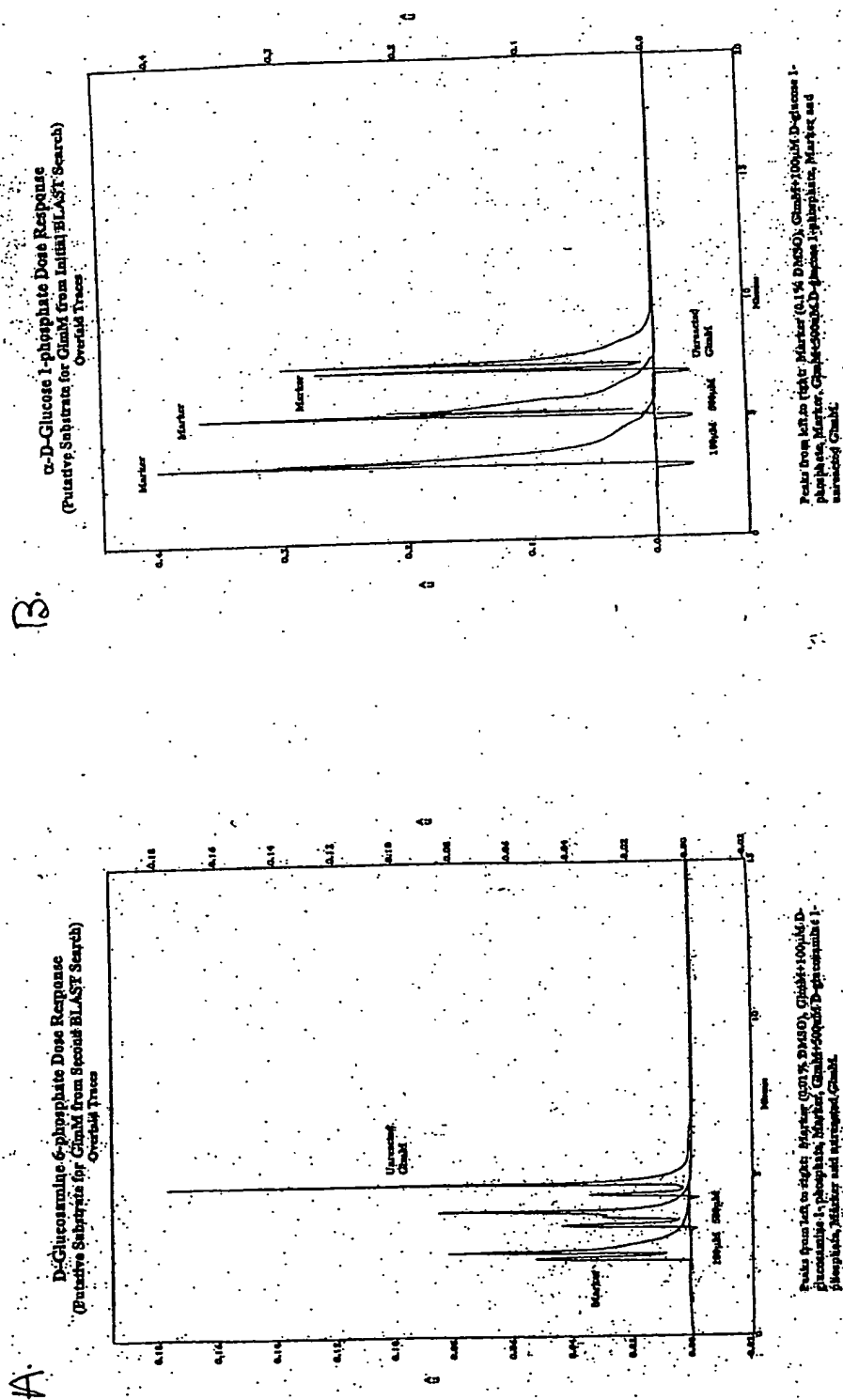


FIGURE 15

C:

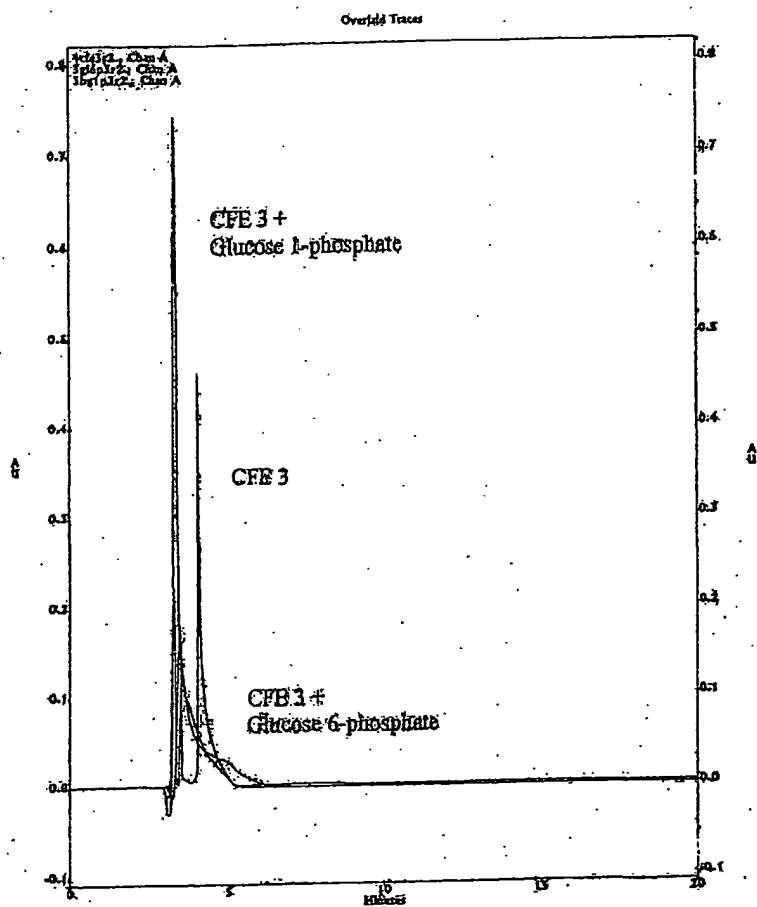


FIGURE 15

D.

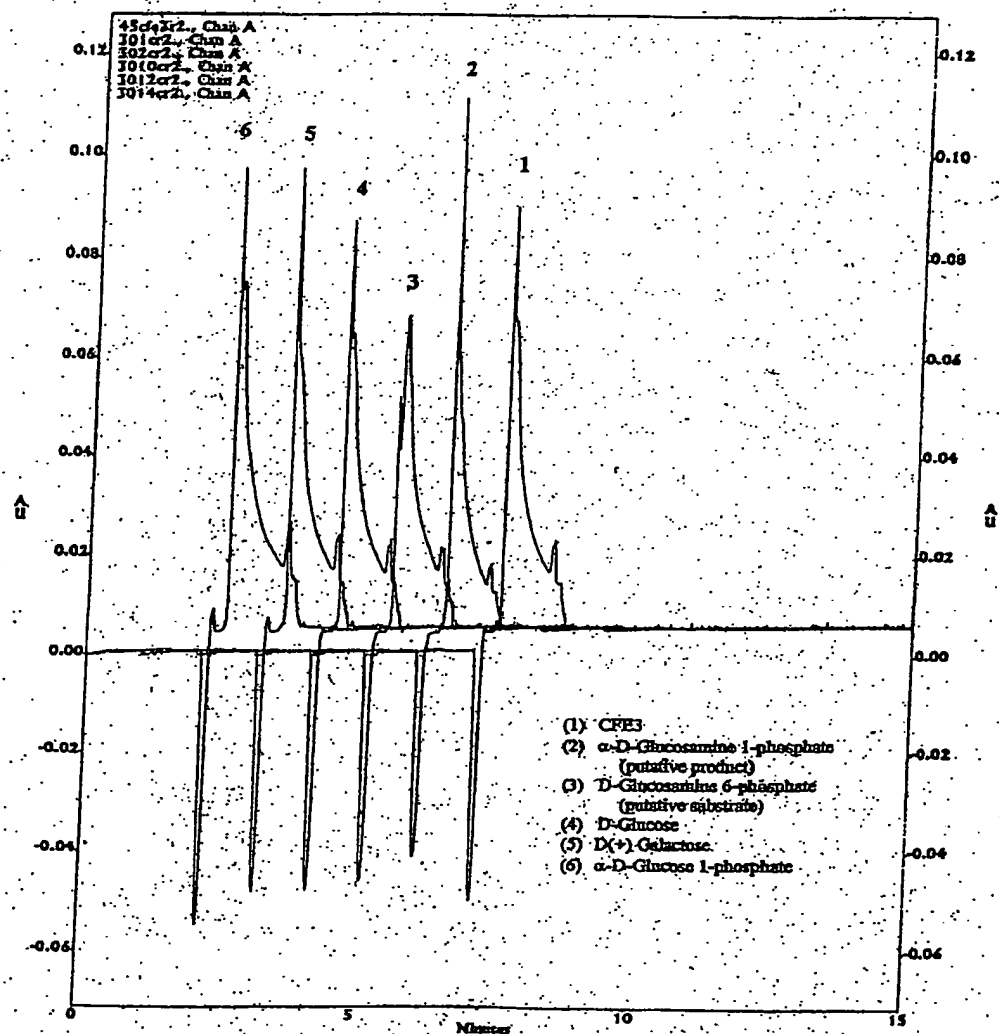


FIGURE 15

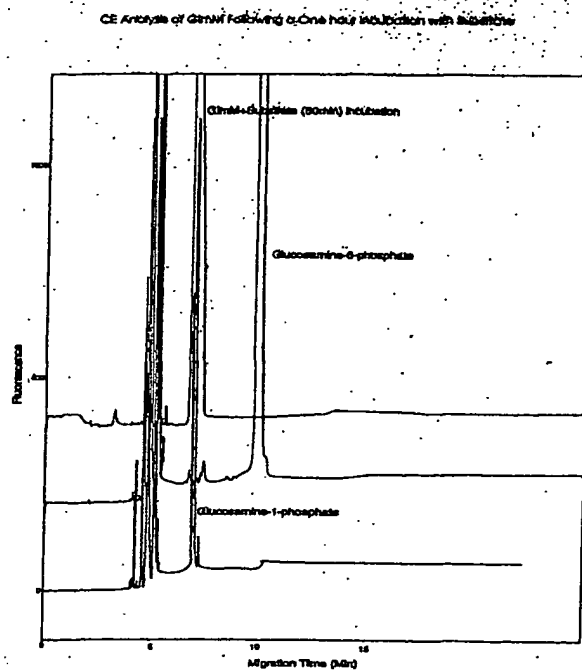


FIGURE 16



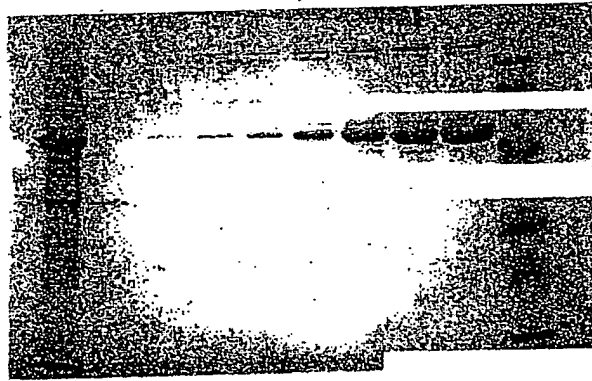


FIGURE 17

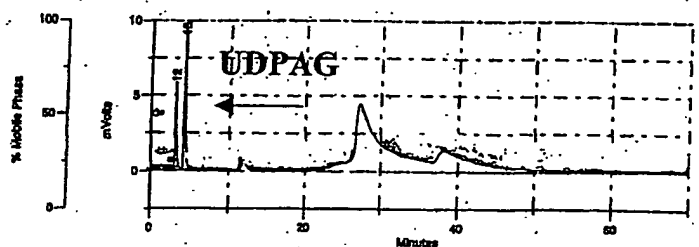


FIGURE 18

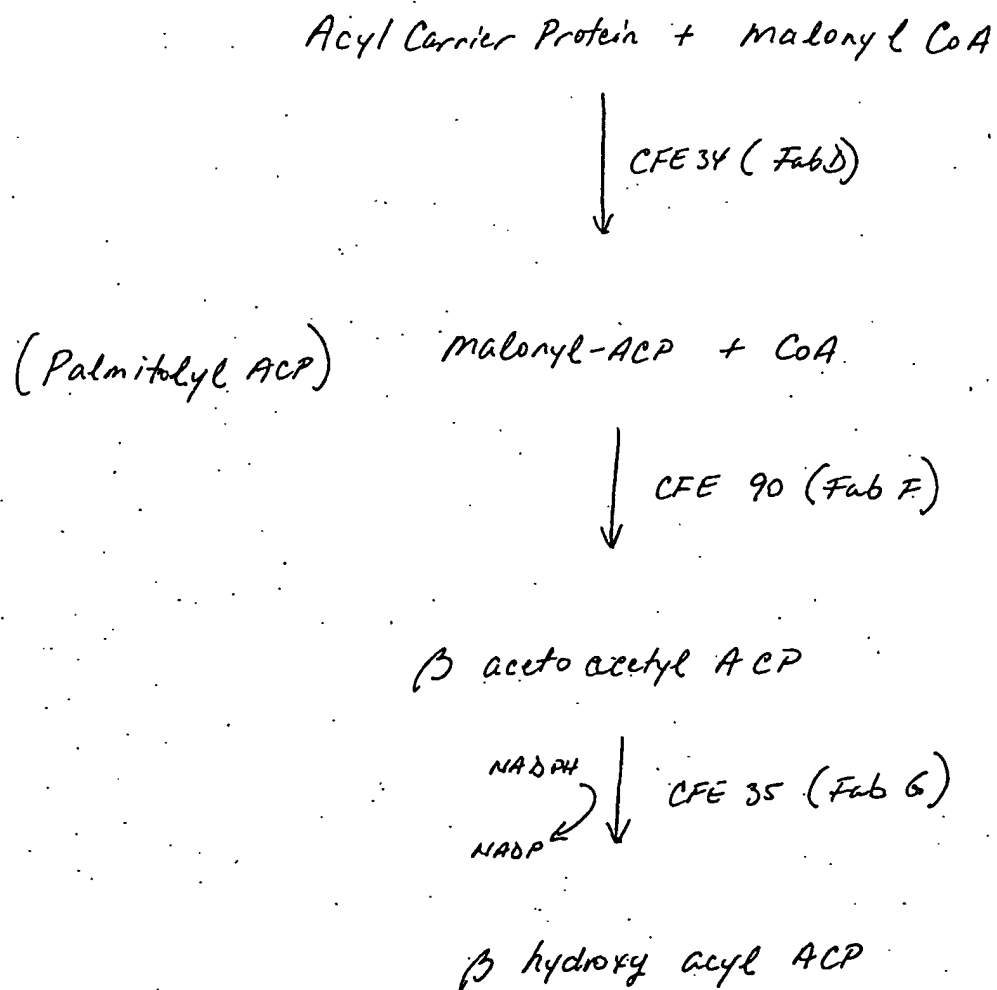


FIGURE 19.

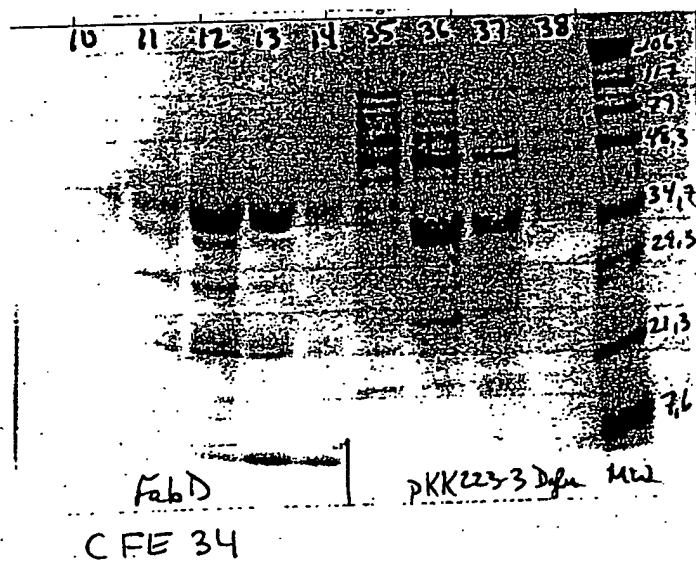


FIGURE 20

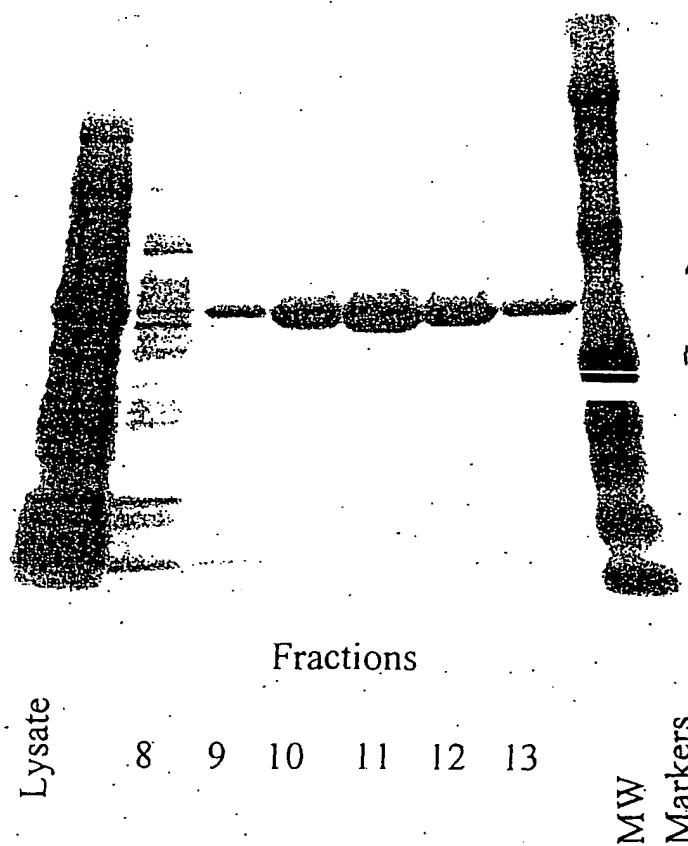


FIGURE 21

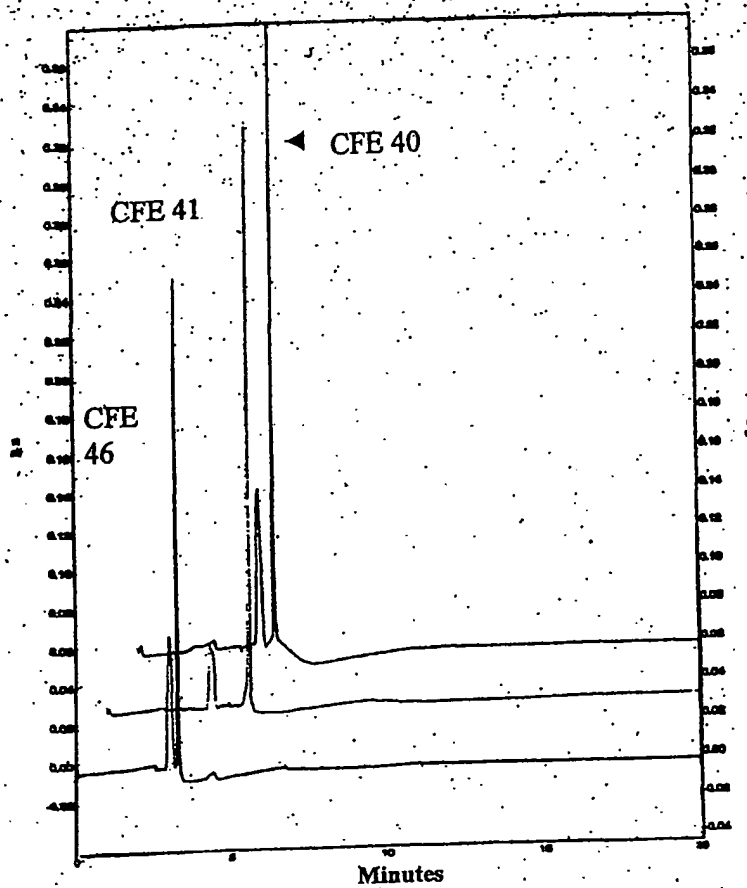


FIGURE 22

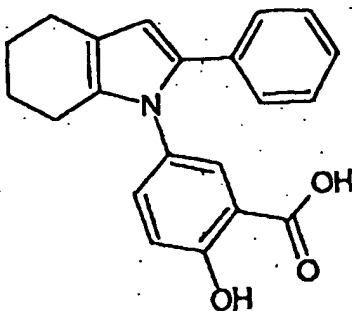


FIGURE 23

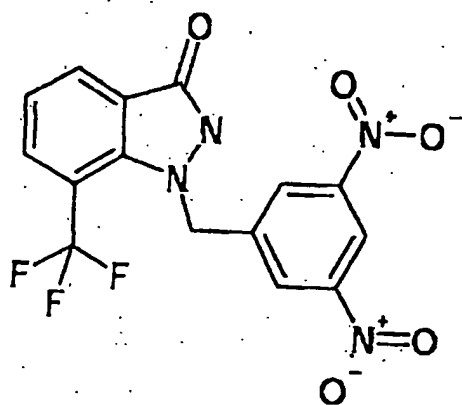


FIGURE 24



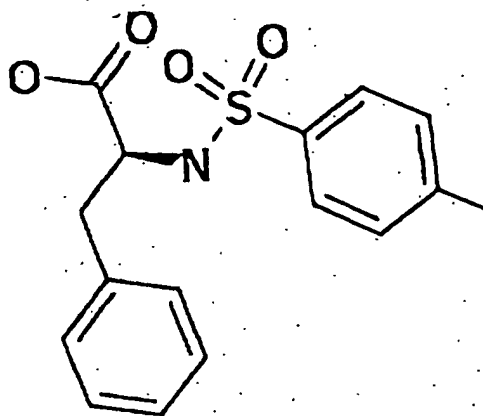


FIGURE 25

2 CFE1 "homologue of SEQ. ID NO. 1"

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 AAAATTGTAGTTGGTGTTCATGGAGACTGGGTTTCTCATGCAGAAQATCTTGTAGATAAATATCTTCCTCT  
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 TCAAGGACAAACACCTCAAACATTCCGTTGCAAGGACTTCATGGACCTTTATGGATCTCTTCTGATGAA  
 GAGAAAGAAAATCTTGACAGATGCATGTAAAATCTTTGTGATCAAAGGAAAAGATGTGGCTTTGGCCAAA  
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 GACTAG

2 CFE2 "homologue of SEQ. ID NO. 2"

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 GCTTCTGTGATTCGCTTGGTTATCCAGCTCTTACAGAAGAACTCGTCTGTGACCTTGCTAAAGAAAGTGA  
 AGAAGGTCGGGCGAAAATGCTAAAGTGGCTGTCCGCAATATCCGTCGCGATGCTATGGACGAAAGCTAAGA  
 AACAAAGAAAAGCAAAAAGAAATCACTGAAGACGAATTGAAAGACTCTTGAAAAAGATATTCAAAAAGTA  
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2 CFE3 "homologue of SEQ. ID NO. 3"

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 ACCTGACACACGTAATTCAGGGGAAATGCTGGAATCGGCCCTTGGTGGCAGGTCTCTTTCACTAGGAGATT  
 CAGGTATACAAACTTGGTGTCTTGGCAACACCAGCAGTAGCTTACTTGGTTGAAACTGAAGGAGCAAGTG  
 CCGGTGTCATGATTTCTGCTAGCCACAACCCAGCCCTTGATAACGGAATCAAATCTTTGGCGGTGATGG  
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 CTGTTTCAACTGGAACCTCTTGTATGGAATGAAGGTTGCCCTTGGATACAGCTAATGGAGCAGCTTCTAC  
 CAGTGCCCGTCAAAATCTTTGCAGACCTTGGTGCCCAATTGACGGTTATCGGGGAAACACCCAGACGGTCTT  
 AAGATCAACCTTAATGTTGGTTCAACACATCCAGAAGCCCTTCAAGAAAGTGGTCAAAAGAAAGTGGGTCA  
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 ACTGCAGTTGGTGACCGCTACGTTGTTGAAAGAAATGAGAAAAATCAGGTTACAACCTTGGTGGTGAACAGT  
 CTGGTACGTTATCTTGATGGATTACAATACCACAGGTTGATGGTCAATTATCAGCAGTTCAATTGACTAA  
 AATCATGAAGGAAACTGGTAAAGAGCTTATCAGAGTTGGCGGCAGAAAGTAACGATTTATCCACAAAAATT  
 AGTTAATATCCGAGTGGAAAACGTCAATGAAGGAAAAGGCCATGGAAATGCCAGCTATCAAGGCCATCAT  
 CGAGAAATGGAAGAAAGAAATGGCGGGGAACGGCCGTATCCTTGTTCGTCCAAGTGGAAACAGAACCCCT  
 CTTGCGTGTATGGCAGAAGCGCTACAAACAGAAGAAGTAGACTACTATGTTGATACCATCACAGATGTA  
 OTTCGTGCTGAAATTTGGGATTGACTAA

2 CFE4 "homologue of SEQ. ID NO. 4"

## 2CFE 4 homologue of SEQ ID NO: 4

Fig. 29  
 ATGAAAAAATACTAATTGTAGATGATGAGAAACCAATCTCGGATATTATCAAGTTTAAATATGACCAAGG  
 AAGGTTATGAAGTTGTAAGTCTTTTAAATGGTTCGTGAAGCGCTAGAGCAATTTGAAGCAGAGCAACCAGA  
 TATTATTATTCTGGATTGTATGCTTCCAGAAAATGATGGTTTGAAGTTGCTAAGACCAATCGTAAGACAA  
 GCAGTTGCCCCATTCTTATGCTTTCAGCCAAAGATAGTGAATTTGATAAGGTTATCGGTTTGGAACTTGGG  
 GCAGATGACTATGTAACGAAACCCCTTCTCCAATCGTGAGTTGCAGGCGCGTGTAAAGCTCTTCTGCGTC  
 GTTCTCAACCTATGCCAGTAGATGGTCAGGAAGCAGATAGTAAACCTCAACCTATCCAAATTGGGGATT  
 AGAAATGTTCCAGACGCTACGTGGCTAAAAATATGCGGAAGAAGTACTAGACTTAACCATCCTGAAATTT  
 GAGCTTTTGTATCATTTAGCACCGCATACAGGTCAAATCATCACGCGGAACACTTGTCTGAGACTGTCT  
 GGGGTTATGACTATTTTGGTGATGTCCGACAGTTGATGTGACTGTACGACGTCTCGTGAGAAAGATTGA  
 AGATAAGCCGACCGACAGAGTATATCTTGACGCGCGTGTGTAGGGTATTACATGAGAAATAATGCT  
 TCA

## 2CFE 5 "homologue of SEQ. ID NO. 5"

Fig. 30  
 ATGGAAGAAATTCCTCTGTATTGGTTGTGGAGCAACCATTACAGACGACAGATAAGGCTGGTCTTGGTTTTA  
 CCCCCAGTTGGCACTTGAAAAAGGTTTGGAGACTGGCGAAGTCTATTGCCAACGCTGTTTCCGTCCTCCG  
 CCACTACAATGAAATCACAGATGTCCAGTTGACGGACGATGATTTCTCAAGCTCTTGCACGAGGTGGGA  
 GACAGTGATGCTTTAGTGGTCAATGTCTATTGATACTTTGATTTTAATGGATCTGTATCCAGGTTTACC  
 AGGTTTTCGTCCTCGGGCAATGATGTCTCTTGGTAGGAAATAAAAAAGATATCCTTCTCAAGTCAAGTAAAG  
 TCTGTTAAGATTAGCCAGTGGCTCATGAAACGTGCCATGAAGAAAGGCTTCTGCTCCAGTCCATGTGGTCC  
 TCACTTCAGCAAAAAATAAATATGCCATTAAAGGAAAGTCAATTGATAAGATTGAACACTACCGTAAGGGCC  
 GCGATGCTCTATGTGGTGGTGTGACCAACGTTGAAAAATCAACTCTAATCAATGCTATTATCCAAAGAAAT  
 CACGGCTGATCAGAATGTCTACTACTTTCACGCTTTCAGGGACAACCTTGGACAAAAATAGAGATTCCG  
 CTGACGACCGATCTTATATTTACGATACGCGCGGAATTATCCACCGCCACCAAGTGGCTCACTACTTGA  
 CGGCCAAAAACCTCAAGTATGTCTAGTCTAAAAAGGAAATCAAGCCTAAGACCTATCAGCTTAATCTGGA  
 GCAAAACCTATTTTAGGTGGTTTGGGACGCTTTGACTTTATAGCAGGAGAAAAAGCAAGGATTACTGCT  
 TTCTTGATAATTGAACTCAAACTCCATCCTAGCAAGCTTGAAGGAGCTAGTCTTCTACGATAAGCAAC  
 TGGGAAGCTCTCTGACACCAACCAATAGCAAGGAAAAAGAAAGATTTCCTCAAGCTAGTCCAGCATGTCTT  
 TACCATTAAAGATAAGACAGACCTAGTCAATTCAGGCCTAGGCTGGATTCTGTAAACAGGCATAGCAAAA  
 GTGCGCTGTGGGCACCAAGGCGCTCGCGCTGTCACAGCAAAAGCAATTATTTAA

## 2CFE 6 "homologue of SEQ. ID NO. 6"

Fig. 31  
 ATGTATCCAGATGATAATTTGACATTGCACACGGACTTGTACCAAGATCAACATGATGCAGGTTTACTTTG  
 ACCAAGGGATTACAAATAAGAAGGCGGTCTTTGAGGTGATTTCCGCCAACAGCCTTTAAGAACCGCTA  
 TGGGTTTTCAGGTTTGGAAAGAATTGTGAACATCTTGAAGACTTGGCTTTTTCAGATAGTGATATAAG  
 CCTATTGGAGTCGCTTGGTTATCATGGGGCTTCTGGATTACCTTCGCAATTTCAAGTTGGAGTTGACC  
 GTTGGTTCTGCGCCAGAAAGGGGATTGGTTTGTCAATGAACCGATTGTGACAGGTGGAAGGACCTCTAG  
 CCAATGTCAGTTGGTTCGAAACGGCTCTTTGAACATCGTCAACTACCAGACCTTGGTGGGACGAAAGGC  
 AGCTCGTATTGCTTCGTTATCGAAGATGAACCTTGTATGGAATTTGGGACACGTCGGGCTCAAGAAATG  
 GATGCGGCCATCTGGGGAACACGCGCAGCTGTGATTGGTGGCGCCAATGGAACAGCAACGTCGTGCG  
 GGTAAAGCTCTTTGACATTCTGTTTGGGAACCCAAGCCATGCGCTTGGTACAGGTTTATGGCAATGACTA  
 TGAAGCTTCAAGGCTTACGCTGCGAACCACAAAAATGTGTCTTCTTGTGGATACTATGACACCTTC  
 GCATCGGTGTACAGCTGCCATTACAGGTGGCGCOTGAGCTGGGTGATTAGATTAACTTTATGGGTGTGCG  
 GATTGACTCTGGGATATTGCTACATTTCTAAGAAAGTCCGTCAGCAACTGGACGAGGCTGGATTTACA  
 GAGGCTAAGATTTATGCTTCTAATGATTTGGACGAAAAATACTATCCTCAACCTCAAGATGCAAAAGGCCA  
 AGATTGATGCTGGGGCGTGGGTACCAAGCTGATTACAGCCTATGACCAGCCAGCTCTTGGGGCGGTTTA  
 CAAGATTGTTCAATGGAAGATGAACCTGGTCAGATGCGCAATACGATTAAGCTGTCTAATAATGCGGA  
 AAAAGTGTCCAGCGCCAGGTAAGAAGCAAGTGTGGCGCAATTACAGTCTGTGAAAAAGGCAAGTCAGAAG  
 GTGACTACATCACTTATGATGGTGTGGATATTAGCGACATGACAGAAATCAAGATGTTCCATCCGACCTA  
 TACATACTCAAGAAACGGTTCGTAATTTTGTATGCCGTTCTCTCTTGGTGGATATCTTCAAGAAAGGTA  
 TATTAGTTTACAACCTTGCTAGTTTGAAGTACATTCAGGATTATGCCCGTAAGGAATTTGACAAGTTGTGG  
 GATGAGTATAAGCGTGTGCTCAATCCGACGACTATCCAGTGGATTGGCGCGTGTATGTATGGCAAGATA  
 AGATGGACTTGAATTGATAAGATGCGCAAGGAAGCCCTTGGTGAAGGAGAAGAAAGATGA

## 2CFE 7 "homologue of SEQ. ID NO. 7"

Fig. 32  
 ATGGCTACTATTCAATGGTTTCTTGGTCACATGTCTAAAGCGCGTGGACAGGTGCAGGAAAAATTTAAAT  
 TTGTTGATTTTGTGACGATTTAGTAGATGCACGCTTGCTCTATCTAGTCAAAATCCTATGTTGACCAAG

## 2CFE 7 (cont'd)

ATTGTTGGTGATAAAACCAAACTCTTGATTTTAAACAAGGCCGACTTGGCTGATCCAGCAATGACCAAGG  
 AATGGCGTCAATATTTGAATCACAAGGAATCCAGACGCTAGCTATCAACTCCAAAGAGCAAGTGACTGT  
 AAAAGTTGTAACAGATGCGGCCAAGAAGCTCATGGCTGATAAGATTGCTCGCCAGAAAGAACGTGGGAT  
 TCAGATTGAAACCTTGGGTACCATGATTATCGGGATTCCAAACGCTGGTAAATCCACTCTGATGAACCGT  
 TTGGCTGGTAAAGATTGCTGTTGTTGGAAACAAGCCAGGGGTACAAAAGGTCAACAATGGCTTAAA  
 ACCAATAAAGATCTGGAAATCTTGGATACACCGGGGATTCTCTGGCCTAAGTTTGAGGATGAAACTGTTG  
 CACTTAAGTTGGCATTGACTGGAGCTATCAAGGATCAGTTGCTTCTTATGGATGAGGTTACCATTTTTGGT  
 ATCAATATTTCAAAGAACATTATCCAGAAAAGCTGGCTGAACGCTTCAAACAAATGAAAATTGAAGAA  
 GAAAGCGCTGTGATTATTAAGATATGACCCGCGCCCTCGGTTTCGGTGATGACTATGACCGTTTTTACAG  
 TCTGTTGGTGAAGGAAGTCCGTGATGGCAAACTCGGTAACTATACCTTAGATACATTGGAAGACCTCGAT  
 GGCAACGATTAA

## 2CFE8 "homologue of SEQ. ID NO. 8"

ATGATTAACAATGTTGTACTTGTAGGGCGTATGACACGTGACGCTGAGTTGCGTTATACCCCATCAAATG  
 TAGCAGTTGGCACTTTTACTCTTGCAGTAAACCGTACATTTAAGAGTCAAAATGGTGAACTGAGGCTGA  
 TTTATGAATGTCGTTATGTGGCGCCAACAGGCTGAAAATCTTGCTAACTGGGCTAAAAAAGGCTCACTT  
 ATCGGGGTGACAGGTCGTATCCAGACTCGTAGTTACGATAACCAGCAAGGACAACGTTCTACGTGACA  
 GAGGTGTTGGCTGAAGAAATTTCCAAATGTTGGAAAGCCGTAGTGTGCGTGAGGGTCAACAGGTGGAGCT  
 TACTCTGCACCAACTGCAAACTATTACGACCTACAAATTCAGTACCAGACTTTTACGTAATGAAAATC  
 CATTTGAGCAACAAACCCATTGGATATTTAGATGATGATTACCATTTCTAA

## 2CFE9 "homologue of SEQ. ID NO. 9"

ATGAAAACGCGTATTACAGAAATTATTGAAGATTGACTATCCTATTTTCCAAGGAGGGATGGCTGGGTTG  
 CTGATGTTGATTTGGCAGGGGCTGTTTCCAAAGGCTGGAGGATTAGGAATTATCGGTGGGGGAAATGCCCC  
 GAAAGAAGTTGTCAAGGCCAATATGATAAAATCAAATCATTGACTGATAAAACCTTTGGGGTCAACATC  
 ATGCTCTTATCTCCCTTGTGGAAAGATATCGTGGATCTCGTTATTGAAGAAAGGTGTTAAAGTTGCACAAC  
 AGGAGCAGGAAATCCAAGCAAGTATATGGAACGTTTCCATGAAGCTGGGATAATCGTTATTCCTGTCTT  
 CCTATGTCGCTTTAGCTAAACGCATGGAAGAAATCGGTGCGAGCGCTGTTATTGCAGAAAGGAATGGA  
 GCTGGGGGGCATATCGGTAATTAACAACCATGACCTTGGTGGCAGAGGTAGCCACAGCTGTATCTATTC  
 CTGTTATGCTGCAGGAGGAATTGGCGATGGTGAAGGTGCTGCGGCTGGCTTTATGCTAGGTGCAAGGC  
 TGTACAGGTGGGACACGCTTTGTAGTTGCAAAAGAGTCGAATGCCATCCAACTACAAGGAGAAAAT  
 TTAAAAAGCAAGGATATTGACACTACGATTCAGCTCAGCACTTTGGTCATGCTGTTCTGCTATTAAAA  
 ATCAGTTGACTAGAGATTTTGAAGCTGGCTGAAAAGATGCCTTAAGCAGGAAAGATCCTGATTTAGAAAT  
 GTTGAACAAATGGGAGCAGGTGCCCTAGCCAAAGCAGTTGTTACCGGTGATGTGGAGGGTGGCTCTGTC  
 ATGCGCAGGTCAAATCGCAGGGCTTGTTCCTAAAGAAAGAAACAGCTGAAGAAATCCTAAAAAGATTTGTATT  
 ACGGAGCCGCTAAGAAAATTCAGAAGAAAGCCTCTCGCTGACAGGAGTTGTAAGAAATGACTAA

## 2CFE10 "homologue of SEQ. ID NO. 10"

ATGATCGATATTCAAAGGAATCAAAGAAGCTCTTCCCCACCGTTATCCTATGCTTCTAGTGGACCGTGTCTT  
 GGAAGTGAGCGAGGATACCATTTGTTGCTATCAAAATGTGACCATTAACGAACCTTTCTTTAACGGCCAC  
 TTTCTCAATAECCAGTTATGCCAGGTGTTCTGATTATGGAAGCCTTGGCCCAAACTGCTGGTGTGTTGGA  
 GTTATCAAAACCTGAAAAATAAGGAAAACTGGTCTTTACGCTGGTATGGACAAGGTTAAGTTCAAGAA  
 GCAAGTTGTACCAGGGCGAACATTTGGTTATGACAGCGACTTTTGTAAACGTCGTGGCACCATAGCTGTG  
 GTTGAACCAAGGCTGAAGTGAATGGCAAGCTTGACGCCAGTGGTATCCTTACTTTTGAATTGGGAAC  
 AA

## 2CFE11 "homologue of SEQ. ID NO. 11"

ATGATTATCAAAATTTATCAACTAACTAAGCCTAAGTTTATCAATGTCAAATATCAGGAAGAGGCTATTG  
 ACCAAGAGAAATCATATCCTTATCCGTCCCACTACATGGCTGTCTOTCATGGGATCAGCGTTACTATCA  
 GGGAAAAAGTGATCCCAAGATTTGAATAAAAAAGCTTCCAATGGCAATGATTACAGAGTCATGTGGAAC  
 CGTCAATTTCTGACCCGACCGGAACCTACGAGGTTGTCAAAGATTTGTCATGATTECCAATCAGTCTCT  
 ATGACAGAGTGATGAAGAAATTCATGAAAACTACATGACAGGGACCCATTCTTGTCTAGTGGATTGTATG  
 GCTTTATGAGAGAGTTTGTCTCTCCCTAAAGATCGTGTGGTGGCTTATGATGCTATTGAAGATACGGTT  
 GCAGCCATTACGAGTTTGTGAGTGTGGGCAACGCTATGAATCGTCTATTGACTCTTGCTCATAGCA  
 AGCGGAGCGGATCGCGTTATTGGAGATGGAAGTTTAAAGCTTTGTGGTTGCCAATATTAACAATACTAC  
 TTTCCTCAAGAGCAGAGATTGTGTTATTGGTCTGATTTGGGAAAAAGTTGGAAGCTCTCTCATTTGCCAAA

Fig. 36 (contd.)

2 CFE 11 (Contd.)

GAATGGTATATTACGGATAATATTCCTGAAGATTGGCCCTTGACCATGCTTTTGAATGTTGTGGTGGTGA  
 TGGTACTGGACCAGCTATTAATGACTTGATTGCGTACATTCGTCCTCAGGGAACGATTCTCATGATGGGA  
 OTTAGGGAATATAAAGTCAATCTCAATACTCGCATGCCTTAGAAAAGGGCTTGATTTTGGTTGGGTCTAT  
 CTGGTTCTGGTGGCATTGATTTTGAATAATGCTATCCAAATGATGGAAGTCAAGAAATTTGCCAATCGTCTT  
 AAAAAATATCCTTTATCTAGAAGAAGCTGTAAGAGAAATTAAGATATTTCATCGTGTCTTTGCAACCGATT  
 TAAACACAGCCTTTAAAAACAGTGTTAAGTGGGAAGTATAA

Fig. 37

2 CFE12 "homologue of SEQ. ID NO. 12"

ATGAACCTTAAAACTACTTTGGGCCCTTCTTGCTGGGCGTTCTTCCCACTTCGTTTTAAGCCGCTTTGGACG  
 TGAACTACGCTCCCAGGGAAGTCCGCTTCAATTTGATAAAGATATTTACAAAGCCTAGCTAAGAAC  
 TACGAGATTGTCTGTGCTACTGGAACAAATGGAACCAACCTGACAACTGCCCTCACTGTGCGCATTTAA  
 AAGAGCTTTATGGTCAAGTTCTAACCAACCAAGCGGTGCCAATGATTACAGGGATTGCAACAACTT  
 CTTAACAGCCAAATCTTCAAAAACTGGGAAAAATATTGCGCTCTCGAAATTGACGAAGCCAGTCTATCT  
 CGTATCTGTGACTATATCCAGCCTAGTCTTTTGTCACTAATACTCTCCGTGACCAAGATGACCGTTTC  
 CGTGAAATCTTATCTACTACCTATAACATGATATTGGATGCCATTGCAAAAGTTCCAACTGCTACTGTTCTCT  
 TAACGGAGACAGTCCACTTTTCTACAAGCCAACTATTCCAAACCTATAGAGTATTTTGGTTTTGACTTGG  
 AAAAAGGACCGCCAACTGGCTCACTACAATACCGAAGGGATCTCTGTCTGACTGCCAAGGCATCTCT  
 CAAATATGAGCATAATACCTATGCAAACTTGGGTGCTATATCTGTGAAGGTTGTGGATGTAAACGTCCT  
 GATCTGACTATCGTTTGAACAACTGTTGAGTTGACCAACAATCGCTCTCGCTTTGTCTAAGACGGCC  
 AAGAAATACGGTATCCAAATCGGGCGGCTCTATAATCTATAACGCCCTAGCTGCTGTGGCCATCGCCCG  
 TTTCTAGGTGGCATTGCAACTCATCAACAGGGATTGACAAGAGCCGTGCTGTCTTTGGACGCCAA  
 GAAACCTTTCTATCGGTGACAAGGAATGTACCCTTGTCTTGATTAAAAATCCAGTCCGTGCAACCCAAAG  
 CTATCGAAATGATCAAACTAGCACCTTATCCATTTAGCCTATCTGTCTCTCTAATGCCAACTATGCAGAT  
 GGAATGACACTAGCTGGATCTGGGATGCAGACTTTGAACAAATCACTGACATGGACATTCCTGAAATCA  
 ACGCTGGCGGTGTTCTCATTCTGAAATCGCTCGTCCCTCCGAGTGACTGGCTATCCAGCTGAGAAAAAT  
 CACTGAAACGAGTAATCTGGAGCAAGTTCTCAAGACCATTGAGAATCAAGACTGCAAGCATGCCTATATT  
 CTGGCACTTATACTGCCATGCTGGAATTTCTGTGAACCTGCTGGCTAGTCTCAGATTGTTAGAAAGGAGA  
 TGAACCTAA

Fig. 38

2 CFE13 "homologue of SEQ. ID NO. 13"

ATGGTTTATACCTTCACTTTTCTCAAAAAGATGGCAATTACCCCTATCAGCTCAACATTGCCACCTCTACGG  
 AAATCTCATGAATACCTACGGGGACAATGGAACATCCTCATGCTCAAGTATGTGGCTGAAAAAAGCTGGG  
 AGCCCATGTGACCGTTGACATCGTTTCTCTCCATGATGACTTTGATGAAAAATCACTACGACATCGCCTTT  
 TCGGTGGTGGTCAAGACTTTGAACAAAGTATCATTTGACAGCGACCTACCTGCTAAAAAAGAGAAGCATTTG  
 ACAACTCATCCAAAACGACGGTGTAGTTCTGGCTATCTGCGGTGGTTTCCAACTATTGGGTCAATATTAT  
 GTTGAAGCTTCAGGAAAAACGTATCGAAGGGCTAGGGGTGATGGGACACTACACGCTCAACCAAGCAAT  
 AACCGTTTATCGGTGACATCAAGATTCACAAAGAGATTTGATGAAACCTAGTATGGATTGAAAAATC  
 ACCAAGGCCGTACCTTCTCTGATGACCAAAAAACCGTGGGACAGGTTGTCTATGGAATGGAACAA  
 CGAAGAAAGGTGGTGAAGGGGTTCAATATAAGAAATGCTTTGGTTCTACTTCCACGGGCTATCTCTC  
 TCTGTAATGCCAATCTGGCTTATCGCCTAGTTACTACTGCCCTCAAGAAGAATATGGTCAGGACATCC  
 AACTCCCTGCCATGAGGATATCCTCAGCCAAAGAAATCGCTGAAGAGTACAGTGACGTCAAAAGCAAGG  
 CTGACTTTCTTAA

Fig. 39

2 CFE14

ATGAATGTAAAGAAAAATACAGAACTTGTTTTTCGAGAAGTTGCAGAGGCTAGTCTGAGTGCTCATCGAG  
 AQAATGTTCTGGTCTCTGTGATTCAGTTATCAAOTATGTAGATGTACCGACAGCGGAAGCTTCTTCC  
 GCTAAGTGTCTCATATCGGTGAAAAATCGTGTAGATAAGTTTCTGGAAAAATATGAAGCTTTAAAAAGAT  
 CQAGATGTGACTTGGCATTGATTGGTACCTTCCAAAGACGTAAGGTGAAAGATGTCTTCAATACGTTG  
 ATTATTTCCATGCTTGGACTCAGTAAAGCTAGCAGGGGAAATTCAAAAAAGAGTGACCGAGTCAATCA  
 AGTGTCTCTTCAAGTAAATATTCTAAAGAAGAAAGCAAAACACGGTTTTTCGAGAGAGGAACCTGCTGGA  
 AATCTTGCCAGATTAGCCAGACTAGATAAGATTGAATATGTTGGTTTAAATGACGATGGCACCTTTTGAG  
 GCTAGCAGTGAACAGTTGAAAGAGATTTTCAAGGCCGGCCCAAGATTTACAAAGAGAAATCAAGAGAAA  
 CAAATTCCAAATATGCCTATGACCGAGTTAAGTATGGGAATGAGTCTGATTATAAAGAAGCGATTCAAT  
 TCGTTTCACTTTTGTCTGATAGGTACATCAATTTTAAAGTAG

## 2 CFE15 "homologue of SEQ. ID NO. 15"

ATGGGATTGCTCTAGAAAATGTGAATTTATATATCAAGAAGGTACTCCCTTAGCTTCAGCAGCTTTGTC  
 GGATGTTTCTTTGACGATTGAAGATGGCTCTTATACAGCTTAAATTGGGCACACAGGTAGTGGTAAATCA  
 AGTATTTTACAACCTCTTAAATGGTTTATTGGTGCCAAAGTCAAGGGAGTGTGAGGGTTTTTGATACCTTAAT  
 CACCTGACTTCTAAAAATAAAGATATTCTGTCAAATTAGAAAAACAGGTTGGCTTGGTATTTCACTTTGCT  
 GAAATCAGATTTTGAAGAAACGGTTTTGAAGGACGTTGCTTTTGGACCGCAAAATTTTGAAGTTTCTG  
 AAGAGATGCTGTGAAGACTGCGCGTGAGAACTGGCTCTGGTTGGAATTGATGAATCACTTTTGATCG  
 TAGTCTGTTTGAAGCTGTCAAGGGGACAAATGAGACGTTTGGCATTCAGGCATACTTGGCATGGAGCCA  
 TGTATATTAGTCTTAGATGAGCCAACAGCTGGTCTAGATCCTCTAGGGAGAAAAGAGTTGATGACCTGT  
 TCAAAAACCTCCACCAGTCAGGGATGACCATCGTCTTGGTAACGCATTGATGGATGATGTTGCTGAATA  
 TGTAAATCAAGTCTATGTAATGAAAAGGGACGTTTAGTAAAGGGGGGCAACCAAGTGATGCTTTCA  
 AGACCTGTTTTTATGGAAGAAGTTCAGTTGGGAGTACGTAAATACGGCCTTTTGTAAACGATTGGCT  
 GATAGAGCGCTGTCAATTAACGATTACCGATTAAAGATAGAGGAGTTCAAGGATCGCTAAATGGATAG

## 2 CFE16 "homologue of SEQ. ID NO. 16"

ATGGATATTCAATTTTAGGAACCGGGGCTGGTCAGCCCTCTAAAGCCCCGCAACGTTTCAAGTCTCGCC  
 TGAACCTCTTGATGAGATTAACGAAGTTTGGCTCTTTGACTGTGGAGAAGGTACGCAAAATCGCATTCT  
 GCAAAACCAATTGACACGTAAGGTGAGCAAAATCTTTATTACCCATCTGCATGGAGACCACATTTTT  
 GCTTTGCGAGTTTCTTTCTAGCGTGCTTTTCAAGCCAAATGAAGAGCAGACAGATTTGGAATCTACG  
 GACCTTAAGGAATCAAGTCATTTGTCTTAACCAAGCCTTCGTGTGTCAGTTTCTCGTCTGCCCTACCGCATT  
 CATTTCCATGATTTGACCAAGATTTCTTGGGTAAAATTCTTGAAACCGATAAAATCACTGTGTATGCAGA  
 GGAGCTGGACCACTATTTTCTGTGTTGGCTATCGTGTGTCATGCAAAAGGATCTAGAAGGGACGCTGGAT  
 GGTGA AAAACTCAAGGCTGCTGTGTTCCGTTCCGCCCGCTTTTGGTAAAATCAAAAACGGCCAGGATC  
 TTGTTTGGAAAGACCGAACTGAAATCAAGGCAGCAGACTATATCTCAGCGCCACGTCCAGGTAAGATTAT  
 CACTATTTTAGGAGACACTCGAAAAACGGGTGCCAGTGTGCGTCTGCTGTCAATGCAGATGTCTAGTT  
 CATGATCCACTTATGGCAAGGGTGAAGAAAAATTGCTCGTAACCATGGTCACTCAACTAATATGCAAG  
 CTGCAGAGTAGCGGTAGAAGCAGGTGCCAAACGCCCTCTACTCAACCATATCAGTGCCCGTTTCTCTC  
 AAAGATATTAGCAAACTCAAGAAAACCGCTGCCACAAATTTTGAATAATGTCATGTGTCAAAAGACTTG  
 GAAGAGTGGAATCTAG

## 2 CFE17 "homologue of SEQ. ID NO. 17"

ATGAGTAATATCAGTTTAAACAACACTTGGTGGTGTGCGTGAGAATGAAAAAATATGTACATTGCTGAAA  
 TTGGAGAGTCEATTTTGTTTGAATGTAGGGTTAAATATCTCGAAAAATGAACAATTAGGGGTCTGATG  
 GGTGATCCAAACATGGATTACCTTTTGAATAATAGCAACCGTATTGCTGGGGTTTTCTTGACCCACGGG  
 ATGCGATGCCATGGTGTCTACCTTATCTCTTGGCAGAGGCTAAAGTTCCTGTATTTGGGTCTGAGTTG  
 ACCATTGAGTTGGCAAAGCTCTTTGTCAAAGGAAATGATGCCGTTAAAGAAATTTAATGATTTCCATGTCA  
 TTGATGAGAAATACGGAGATTGATTTTGGTGGGACAGTGGTTTCTTCTTCCCTACGACTTACTCGGTCCA  
 GAGAGTCTGGGAATTGTCTTGAAGACATCGGAAGGAAGCATCGTTTATACAGGTGACTTCAAATTTGACC  
 AAACGGCTAGTGAATCTTATGCAACTGATTTTGTCTCGTTTGGCAGAGATTGGTCTGTGACCGCGTCTGGC  
 TCTCTCAATGATTTGGGCAATGCAAGACAGCAATTTAGGTGGCTAGTGAAGTGAAGTTAGGGATGAA  
 ATTAAACCAAACTATTGCTOACTGGGAAGGTCGTATCATCGTTGCAGCTGTTCCAGTAATCTTTCTCGTAT  
 TGAAGCAATTTTGAAGCTGCGGATAAAACAGGTCCACGTATCGTCTTGACAGGATTGATATTGAAAAAT  
 ATCGTCCGCAAGCGATTCTGTTTAAAGAGTTGTCTTTAGCCAACGAAATTTCTCTGATTAAGCCATAAG  
 ATATGTTCTCGCTTTGAAGACCATGAGTTGATTATCTTGAACAGGTCTGATGGGTGAACCTATCAATGG  
 AGTTCGTAAAGATGTCGATTGGTGGCCATCGTTATGTAGAAATCAAGGATGGGGACCTGGTCTATATTGCT  
 ACCGGTCCGTCTATTGCTAAAGAACCTTTGTTGGCGGTGTGGAAAAATATGATTTATCAGGCAGGTGGGG  
 TTGTGAAATTGATTACCCAAAGTTTACATGTATCAGGGCACGGAAATGTGCGTGAATTTGACGCTGATGAT  
 CAATCTTTTGCAACCTAAGTACCTCTTCCCTGTCCAAGGGGAGTATCGTGAAGTTGGATGCTCACGCTAAG  
 GCTGCCATGGCAAGTTGGGATGTTGCCAGAACGCATCTTCAATCCTAAAAAGGGGACCAACATGGCTTACG  
 AGAATGCAAGCTTTGTTCCAGCTGGATCGGTTTCAAGCAGGAGATATCTTGATTGATGGGAATGCCATTGG  
 TGATGTTGGAATGTTGTTCTTCTGTGACCGTAAGGTCCTGTGAGAGGATGGAATTTTCACTGCTGCTATTA  
 CAGTCAACCGTCTGAGAAAGAAATTTGGTGTGAGGTCGTGTTTCAACGCGTGGATTTGTTATCTCAA  
 GAAGAGTCCGATATTCTCCGTGAAAGTTTCAAGATTGATTAACCAACCGGTAGAAGAGTATCTTCAAGG  
 AAGTGAATTTGCTGGGCAGATCTCAAAGGTAAGGTTCTGTACAATCTGACCAAGTACCTCTTTGATCAA  
 ACCAAGGCTCGCCAGCCATTTTACCAGTAGTCATGGAAGCAAAATAA

## 2 CFE19 "homologue of SEQ. ID NO. 18"

ATGACAAAQAATTTTCATCATGTAAACGGTCTTACTCCACGAAACGATTGATATGCTTGACGTAAAGCCTG  
 AAGGTATCTACGTTGATGCGACTTTGGGCGGAGCAGGACATAGCGAGTATTTATTAAGTAAATTAAGTGA  
 AAAGGCCATCTCTATGCCTTTGACCAGGATCAGAATGCCATTGACAATGCGCAAAAACGCTTGCCACCT  
 TACATTGAGAAGGGAATGGTGACCTTTATCAAGGATAAATTCCGTCATTTACAGGCACGTTTGCGGGAAG  
 CTGGTTCAGGAAATGATGGAATTTGTTATGCAATTTGGGAGTGTCTAGTCCTCAATTGGACCAGCGTGA  
 GCTGCTTTTCTTATAAAAAGGATGCGCCACTGGACATGCGGATGAATCAGGATGCTAGTCTGACAGCC  
 TATGAAGTGGTTAATCATTATGACTATCATGATTTGGTTCGTATTTCTTCAAATACGGTGAGGATAAATT  
 CTCTAAACAGATTGCGCGTAAGATTGAGCAAGCGCGTGAAGTGAAGCCGATTGAGACAACGACTGAGTT  
 AGCAGAGATTATCAAGTTGGTCAAACTGCCAAGGAAGTCAAGAAGAAGGGTCATCTGCTAAGCAGAT  
 TTCCAGGCTATTGCAATTGAAGTCAATGATGAAGTGGAGCGGCAGATGAGTCCATCCAGCAGGCTATG  
 GATATGTTGGCTCTGGATGGTAGAATTCAGTGATTACCTTTCTTCTTAGAAGACCGCTTGACCAAGCA  
 ATTGTTCAAGGAAGCTTCAACAGTTGAAAGTTCCAAAGGCTTGCTTTCTATCCAGATGATCTCAAGCCC  
 AADATGGAATTGGTGTCCCGTAAGCCAATCTTGCCAAGTGGGAAGAGTTAGAAGCCAATAACCGCTCG  
 CACTCAGCCAAGTTGCGCGTGGTCAGAAAAATTCACAAGCTCGAGCACCACCACCACCACCACTGA

## 2 CFE21 "homologue of SEQ. ID NO. 49"

ATGAOTAGAATTTTAGATAATGAGATAATGGGGGATGAGGAGTTAGTAGAACGCACGCTCCGTCCTCAG  
 TATTTAAGTGAATATATCGGACAGGATAAGGTCAAGGACAGGTACAAATCTTTATTGAAGCTGCCAAAA  
 TGGCGCATGAAGCGCTGGATCATGTGCTCTTATTTGGGCTCCAGGTCTCGGGAAAAAGCACCATTGGCTT  
 TGTTATTGCCAACGAAGTGGGAGTCAATCTTAAGCAGACGTCGGGTCCAGTCATTGAAAAAGCCGGAGAT  
 CTGGTAGCTATTTGAATGAGTTAGAGCCTGGGGATGTCTTTTATTGATGAGATCCATCGTTTCCCAAT  
 GTAGTGGAAGAGGTGCTTTATAGTGCTATGGAGGACTCTACATAGATATTATGATTGGGGCTGGTGAG  
 GGTAGTCTGATGTTTCATTGGAGTTACCACTTTTACCTTGATTGGTGCGACGACTCGGGCTGGTATGCT  
 CTCCAACTCGGTACGGGCACGTTTGGGATTACAGGCCATATGGAATATTATGCCCATGCTGACTTGACA  
 GAAATTTCTGAGCGGACGGCAGATATTTTQAGATGGAATCACTCATGAGGCACGATCTGAGTTGGGCC  
 TAGCTATGCTGGGACCCCTCGTATTGCCAATCGTCTCTCAAGCGCGTGGCGGATTTTGGCCAGATAATG  
 GGAATGGGGTAATTGATGATATTATTACCGATAAGGCTTTGACTATGCTGGATGTTGACCTGAAGGTT  
 TGGACTATGTGGATCAAAAAATCCTTCGTACCATGATGAGATGTACAGTGGAGGACCTGTTGGTCTAGG  
 AACTCTTCTGTGAATATCGCCGAAGAGCGTGAGACAGTTGAAGACATGATGAGCCTTACTTGATTCAA  
 AAAGGTTTATCATGCGGACACGGTCTGGACGGGTGGCGACTGCTAAGGCATATGAGCACTTAGGTTATG  
 AATACAGTGAAGAAAGCGGCCGCACTCGAGCACCACCAGCACCACCACCTGA

## 2 CFE24 "homologue of SEQ. ID NO. 20"

ATCAGTATGTTTTTAGATACAGCTAAGATTAAGGTCAAGGCTGGTAATGGTGGCGATGGTATGTTGCCCT  
 TTCCTCGTGAAGAAATATGTCCTAATGGAGGCCCTTGGGGTGGTGAATGCTGCTCGTGGAGGCAATGTTGGT  
 CTTCGTTGTAGACGAAGGACTACGTACCTTGATGGATTTCCGCTACAATCGTCATTTCAAGGCTGATTCTG  
 GTCAAAAAGGGATGACCAAGGGATGCATGGTGGTGGTGGTGGAGGACCTTAGAGTTGGAATACCACAAG  
 GTACGACTGTTCTGTGATGCGGAGACTGGCAAGGTTTAAACAGATTGATTGAACATGGGCAAGAAATTTAT  
 CGTTGCCACCGTGGTGGTGGTGGACGTGGAAATATTCTGTTTCGCGACACCAAAAAATCCTGCACCGGAA  
 ATCTCTGAAAAATGGAGAACCAAGGTCAGGAACGTGAGTTACAATTTGGAATCAAAAAATCTTGGCAGATGTC  
 GGTTTAATAGGATTCCTATCTGTAGGGAAGTCAACACTTTTAAAGTGTATTACCTCAGCTAAGCCTAAAT  
 TGGTGGCTAACCACTTTACCACTATTGTACCAAAATTTAGGATGTTTGGCACCCAATCAGGTGAATCCTTTG  
 CAGTAGCCGACTTGCCAGGTTTGAATTGAAGGGGCTAGTCAAGGTGTTGGTTTGGGAAGTCAGTTCTCTCCG  
 TCACATCAGCGTACACGTGTTATCCTTCACATCATTGATATGTCAGCTAGCGAAGCCCGTGATCCATATG  
 AGGATTACCTAGGTAATCAATAAAGAGCTGGAGTCTTACAATCTTCGCTCATGGAGCGTCCACAGATTAT  
 TGTAACTAATAAGATGGACATGCTGTAGAGTCAGGAAAAATCTTGAAGAATTTAAGAAAAAATTTGGCTGA  
 AAATTATGATGAATTTGAAGATTACCACTATCTTCCAAATTTCTGGATTGACCAAGCAAGGTCTGGCA  
 ACACTTTTAGATGCTAAGCTGAATTGTTAGACAAGACACCAGAATTTTGTCTACGACGAGTCCGATA  
 TGGAAGAAGAAGTTTACTATGATTTGACGAAGAAGAAAAAGGCTTTGAAATTAATCGTGTATGACGATG  
 CGCATGGGTAATTTCTGGTGAAGAACTCATGAACTCTTAAATAGACCAACTTTGATCGTGTATGAATCT  
 GTCATGAATTTGGCCGTACGTTCTGGTATGGGGGTTGATGAAGCCCTTCGTGCGCGTGAAGCTAAAG  
 ATGGGATTTGGTCCGCAATTGGTAAATTTGAGTTTGAATTTGTAGACCTCGAGCACCACCACCACCACCA

rga

2 CFE25 "homologue of SEQ. ID NO. 21"

Fig 46  
ATGAAGTACTTTAATGTTGGGAAAATCGTTAATACGCAGGGATTACAGGGTGAGATGCGAQTCTTGCTG  
TGACGGATTTTGCAGAAGAACGGTTTAAAAAAGGAGCTGAGCTGGCTTTGTTTGATGAAAAAGATCAGTT  
TGTCACAAACATGACCATCGCTAGCCACCGTAAACAGAAGAACTTTGACATTATTAATTCAAAAGATATG  
TACCATATCAATACTATCGAAAAGTACAAGGGATACAGTCTCAAGGTGCGTGAGGAAQATTTGAATGAC  
CTAGACGATGGTGAATTTTACTATCACGAGATTATCGGTTTGAAGTCTATGAGGGTGATAGCTTGOTTG  
GAAACATCAAGGAAAATCCTGCAACCAGGTGCTAATGATGTCTGGGTGGTCAAACGAAAAGGCAAAACGTG  
ATTTCCTTTTACCTTATATCCACCAAGTGGTCTCAATGTTGATATTCCAAATAAACGGGTGATGTGGAA  
ATCTTAGAAGCGTTAGACGATGAAGATCTCGAGCACCACCACCACCACCTGA

2 CFE26 "homologue of SEQ. ID NO. 22"

Fig 47  
ATDAAGATTGATATTTTAACCCCTCTTCCAGAGATGTTTTCTCCACTGGAGCACTCAATCGTTGAAAAGGC  
TCCAGAAAAAGGGCTCTTGGATATCCAGTATCATATTTTCGAGAAAAATGCTGAAAAGGCCCGTCATGTA  
QATGATGAGCCCTACGGAGGCGGTCAAGGCATGTTGCTCAGAGTACAACCTATTTTCGATTCTTTGATG  
CTATTGAAAAAATAATCCGCGCGTTATTCCTCTCGATCCTGCTGGAAGCAAGTTTGATCAGGCTTATGC  
TGAAAGATTTGGCTCAAGAGGAAGAGCTAATCTTTATCTGTGGGCACTATGAGGGTTATGATGAGCGCAT  
AAGACCTTGGTAACAGATGAGATTTCCCTAGGCGACTATGTTCTCACTGGTGGAGAATTGCGAGCTATGA  
CCATGATGATGCTACAGTTCGCTGATTCGAGAAGTGGCAAGGAGTCTAGCCACCAAGATGATAG  
TTTTCTTCAAGGTCTTTTGAATATCTTCAGTACACACGTCCTATGATTATCGAGGCATGGTCTGCGCAO  
ATGATGATGAGTGGTCACCATGAAAAGATTCTGTCAGTGGCGATTGTACGAGAGTTTAAAGAAAAACCTA  
CGAGCGCAGGCCGGATTTACTTGAACATTATCAACTGACAGTAGAAGAAGAAAAAATGCTGGCAGAAAT  
CAAGAAACAAAGAAAGCGGCGCACTCGAGCACCACCACCACCACCTGA

2 CFE27 "homologue of SEQ. ID NO. 23"

Fig 48  
ATGATTCAGCAAGTAAATTAAGGCTGGTATGACCTTTGAAACAGCTGACGGCAAATTGATTGCGGTTT  
TGGAAGCTAGTCAACCACAAACCAGGTAAAGGAAACACGATCATGCGTATGAAATTGCGTGATGTCCGTA  
CTGGTTCTACATTTGACACAAGCTACCGTCCAGAGGAAAAATTTGAACAAGCTATTATCGAGACTGTCCC  
AGCTCAATACTTGTACAAAATGGATGACACAGCATACTTCATGAATACAGAACTTATGACCAATACGAA  
ATCCCTGTAGTCAATGTTGAAAACGAAATTCCTTTACATCCTTGAAAACCTCTGATGTGAAAATCCAATTCTA  
CGGAACCTGAAATGATCGGTGTACCGGTTCTACTACTGTTGAGTTGACAGTTGCTGAAAACCTCAACCATCT  
ATCAAAAGGTGCTACTGTTACAGGTTCTGTGTAACCAAGCAACGATGGAACTGGACTTGTCTGTAACGTTT  
CAGACTTCATGGAAGCAGGACAAAACTCGTTATCAACACTGCAGAAAGGAACCTACGTTTCTCGTGCCCT  
CGAGCACCACCACCACCACCTGA

2 CFE28 "homologue of SEQ. ID NO. 24"

Fig 49  
ATGGCAATTGAAGTTTAAACAQAACGTTTGCAGAACGTTTAAAAATCTACGTAAAAAAGGAAAAATCT  
CTCAATGTGATGTCCAAGAGGCAACCAAGAAATTCGCTTGGCCTTGCTCGAGGCCGACGTTGCCCTTGGC  
TGTGTAAAGGACTTTATCAAGAAAGTTAGTGAGCGTGCAATCGGGCATGAGGTCAATTGATACACTTAAT  
CCTGCCAACAAGATTATTAATAATCGTTGATGAGGAACTGACAGCCGTTTTAGGTTCTGATACGGCAGAAA  
TTATCAAGTCACTTAAGATTCCAACCATCATCATGATGGTTGGTTTACAAGGGGCTGGTAAAAACAACCTT  
TGCTGGTAAATTGGCCAACTCAAGAAAGAAAGAAATGCTCGTCTTTGATGGTTGCGGCGGATATT  
TATCGTCCAGCTGCCATTGAACAGCTTAAGACCTTGGGACAACAGATTGATGTGCTGTCTTTGCACTTGG  
AACAGAAAGTACAGCTGTTGAGATTGTACGTCAAGGTTTGGAGCAAGGCCAACTAATCATACGACTAT  
GTCTTGAATGATACTGCGGGTCTTTTGCAGATTGATGAGCTCCTCATGAATGAGCTTCGTGATGTGAAAG  
CATTGGCTCAACCAAAAGAAATCTTGTCTGCTGATGCTATGATTGGTCAAGGAGCAGCAATGTTGC  
GCCTGAGTTTAAATGCTCAGTTGGAAGTGACTGGGGTCACTCTTACCAAGATTGATGGCGATACTCGTGGT  
GGTCTGCTCTGTTCTGTTCTGTCACATTACTGGAAAACCAATCAAGTTCACTGGTACAGGTGAAAAGATTA  
CGGACATGAAAACCTTCCACCCAGACCGCATGTCTAGCCGTATCCTTGGTATGGGGGATATGCTCACTTT  
GATTGAGAAAGCTTCTCAGGAATACGATGAACAAAAAGCCCTTGAAATGGCTGAGAAAGATGCGGCAAAA  
CACCTTTGATTTAATGATTTTCATCGATCAATTAGATCAGGTGCAAAATATGGGGCCGATGGAAGACTTG  
CTCAAGATGATTCAGGTATGGCCAACAATCCAGCCCTTCAAAACATGAAGGTGGATGAACGCCAGATT  
GCTGTAAACGTTGCCATTGTGCTTCGATGACACCTGAAGAGCGTGAAAACCCAGATTGTTAAATGCCAA  
GCCGTGCGCGCTGTTCTGCTGTGTTGTAATACATTGCTGCAAGTCAATAAATTCATCAAGGACTTT  
AACAGGCTAAACAGCTCATGCAAGGTGTTATGCTGTTGGGATATGAATAAAATGATGAAGCAAAATGGG  
ATTAAATCAAAATAACCTTCTTAAAAATATGCCAAATATGGGAGGAATGGATATGCTGCTGCTTGAAGGAA



2 CFE 28 (Contd.)

(Contd.)

Fig 49

TGATGGGACAAGGCGGTATGCCTGACTTATCAGCTCTCGGAGGAGCAGGAATGCCAGATATGAGCCAGA  
TGTTCGTGGCGGTTTGAAGGTAAAATTGGTGAATTTGCCATGAAACAGTCCATGAAACGTATGGCTAA  
CAAAATGAAGAAAAGCGAAGAAGAAACGCAAGCGCGCCGCACTCGAGCAACEACCACCACCACTGA

2 CFE29 "homologue of SEQ. ID NO. 25"

Fig 50

ATGTATCTTATTGAAATTTTAAATCTATCTTCTTCGGGATTGTTGAAGGAATTACGGAATGGTTGCCGAT  
TTCCAGTACAGGTCACCTTGATTTTAGCAGAGGAGTTTATCCAATACCAAAATCAAAATGAAGCCTTTATG  
TCCATGTTTAAATGTCGTGATTACAGCTTGGTGCTATTTTAGCAGTTATGGTGATTTATTTTAAACAGCTCAAT  
CCTTTTAAACCGACTAAGGACAAACAGGAAGTTCGTAAGACTTGGAGACTATGGTTGAAGGCTTTGATTG  
CCACTTTGCCCTTACTTGGTGCTTTAAATTTGATGATTGGTTTGTATACCCACTTCCATAACATGGTTTCAO  
TTGCTGTCTATGTTGATTATCTACGGGGTTGCCCTTCATCTATTGGAAAAGCGCAATAAAGCGCGTGCTATC  
GAGCCAAGTGTAACAGAGTTTQACAAGCTTCTTATACGACCGCTTCTATATCGGACTCTTCCAAGTTCT  
TGCTCTTTTACCAGGGACTAGCCGTTTCAGGTGCAACGATTGTGCGGTGGTTTGTAAATGGAACCACTCGTT  
CAGTTTGTAGAGAATTTACCTTCTATCTTGGGATTCCCGTTATGTTTGGAGCTAGTGCCCTTAAAGATTTTC  
AAATTTGTGAAAGCCGGAGAATCTTQAGCTTTGGGCAATTTGTTTGTCTCTTGGTCGCGATGGGAGTAG  
CTTTTCCGGTCAGCATGGTGGCTATTCCGCTTCTTGACCAGCTATGTGAAAAAACAGCACTTCAACCTTTT  
GGTAAATACGGTATCGTGGTGTGTTTGTCTACTTACAGTTTGTCCGTTTATTGTACTCGAGCAC  
CACCACCACCACCTGA

2 CFE30 "homologue of SEQ. ID NO. 26"

Fig 51

ATGGGATTTATTTOACCGTCTATTTCGGAAAAAAGAGAACCTAAAAATCGAAGAAAGTTGTAAGAAGCT  
CTGGAAAAATCTTGATTGTCTGAAGATGTTGATCCTACCTTCACAGAAGTTGAGGAAGTTTCTCAGGAAG  
AAGCAAGAGTTGAAATTTGTAACAAGCTGTGTTCCAAGAAGAGGAAATCCAAGACACAGTTGAAAGAAA  
GTCTGATTTAGAGCCAGTTGTAGAAAGTTCTCAAAAAGAAAGTGGAAAGAAATTTCCCACTCAGAAAGAGG  
GAATACTGAGTTTCTAGAGACTATAGAAGAAAAATATTCTGAAGTTCTTGAACCAAGAAAGGCTCAAGC  
AGAAGAAACCGTTCAAGAAAAATATGACCGCAGTCTTAAGAAAACTCGTACAGGTTTCCGTGCCCGCTT  
CAATGCCCTTCTTCTAACTTCCGCTCTGTTGACGAAGAAATTTTCGAGGAAGTGAAGAACTGCTGATTA  
TGAGTGATGTTGGTGTCCAAGTCGCTTCTAACTTAACGGAGGAAGTACGTTACGAAGCCAAAGCTTGA  
TGCCAAAGAAACCTGATGCACTTCGTGCTGTCATCATTGAGAAATTTGGTTGAGCTTTATGAAAAAGATGCT  
AGCTACGATGAAAGCATCCACTTCCAAGATAACTTQACAGTTATGCTCTTTGTGTTGGTGTGAATGGTGTG  
GGAAAACAACTTCTATCGGAAACTAGCCACCGCTACAAACAAGCTGGTAAGAAGGTCATGCTGGTTG  
CAGCAGATACCTTCGCTGCCGCTGCAAGTACGCTGAGTGAATGGGGCCGACGAGTAGATGTTCCAGT  
AGTAAGTGGACCTGAAAAAGCTGATCCAGCCAGCGTGGTCTTTGATGGTATGGAACGTGCCGTGGCTGAA  
GGTATCGATATTCTCATGATTGATACTGCTGGTCTGTCGAAAAATAAGGATAACCTTATGGCTGAGTTGG  
AAAAGATTGGTTCGATTATCAAAACGTGTTGTGCCAGAAGCAACCATTAACCTTCTTGGCACTTGAATGCA  
TCAACAGTCAAAATGCCCTAGTACAGGCCAAAGAAATTTGAAAAATCACACCTTTAACGGGAATTTGTTT  
TGACTAAGATTGATGGAACGTCTCGAGGAGGTGTGGTTCTAGCCATTGCTGAAGAACTCAATATCTCTGT  
AAAAATGATTGGTTTGGTGAAAAAATCGATGATATTGGAGAGTTTAACTCAGAAAACTTTATGAAAGGT  
CTTTGCAAGGTTTAAATCGCGCGCCGCACTCGAGCAACCACCACCACCACTGA

2 CFE31 "homologue of SEQ. ID NO. 27"

Fig 52

ATGTATTTGAAATGGTAGATGAAACTGGTCAAGTTTCAAAAGAAATGTTGCAACAAACCCAAGAAATTT  
TGGAAATTCAGGCCAAAAATTAGAAAAAGAAACAAAGGAGATGGCAGTCACTTTTGTGACCAATGAGC  
GTATGCTAGAACTTAATCTGGAGTACCGTGACACCGACCGTCCGACAGATGTCATCAGCCTTGAGTATAA  
ACCAGAAATGGAAATTCCTTTGACGAAGAGGATTTGCTTGAAAAATCCAGAAATGGCAGAGATGATGCT  
GAGTTTATGCCCTATATTGGGGAATTTGTCATCTCTATCGATAAGGCTCATGAGCAGGCCGAAGAATATG  
GTACAGCTTTBAGCGTGAATGGGCTTCTTGCCAGTACACGGCTTTTACATATTAACGGCTATGATCAC  
TATACTCCGGAAGAAAGCGGAGATGTTCCGTTTACAAGAAAGAAATTTTGACAGCCTATGGACTCACA  
AGCAACTCGAGCACCACCACCACCACCTGA

2 CFE32 "homologue of SEQ. ID NO. 28"

Fig 53

ATGAGTATTCAGTAATTATTGCCGGTTTTAAGGGAAAGATGGGCCAAGCTGCTTGTTCAGATGGTATTGA  
CTGATCCAGACTTGGACTTGGTGGCAGTTTGGATCCTTTTGAAGTCTGAGTCAAGATGGCAAGCTATTCT  
GTTTTCAAGGAAGAGGCTGATTAGCTGGTTTGAAGCGGATGTCTGGGTAGATTTTACTACTCCAGCTGT  
TGCTTAGGAAAATACACGTTTGTCTTGAAGAAATGGCTTTGCTCCAGTAGTTGGAACGACTGGTTTCACGA

2CFE 32

Fig 53 (contd.)

GTGAAGAAATTGCAGAGCTAAAGAAATTTCTCGTGCCCAAGACTTGGGTGGCCTGATTGCCCTAACTT  
 TCCTTGGGTGCTGTCTTACTCATGCAATTTGCGACGCAGGCTGCCAAATATTTCCCAAATGTGGAGATTA  
 TTGAGCTCCATCATGACAAGAAAAGGATGTCCGAGTGGAACAGCCATTAAAAACAGCTGAGTTGATGG  
 CAGAGTTTCGAGAGTGCATTTCAGCAAGGCGCAGCAGATGAGGAAGAGCTGATTGCTGGTGCTCGTGGTG  
 CTGACTTTGATGGTATGCGCATCCACTCAGTTCGTTTGCCAGGCTTGGTAGCTCATCAAGAAAGTCATCTTT  
 GGCAAATCAGGGAGAAGGGTTGACCTCCGTGATGACTCCTATGATCGCATCTCCTTCATGACAGGAGTCA  
 ATTTGGGAATTAAGAAGTTGTCAAGCGTCATGAGCTTGCTATGGATTAGAACACTTATTACTCGAGCA  
 CCAACCAACCACTGA

Fig 54

2CFE33 "homologue of SEQ. ID NO. 29"

ATGGCAAACAAACAAGATTTGATCGCTAAAGTAGCAGAAGCTACAGAATTGACTAAGAAAGACTCAGCA  
 GCAAGCAGTTGAAGCTGTATTTGACAGCAGTAGCTGACTATCTTGACAGCTGGTGAAGAAAGTTCAATTGATCG  
 GTTTTGGTAACTTTGAAAGTTCGTGAGCGTGCAAGACGTAAGGTCGCAACCCACAACCTGGTAAAGAAAT  
 GACAAATGCAAGCTTCTAAAGTACCAGCATTCAAAGCTGGTAAAGCTCTTAAAGACGCTGTTAAACTCGAG  
 CACCAACCAACCACTGA

Fig 55

2CFE34 "homologue of SEQ. ID NO. 30"

ATGACTAAAAACAGCCTTTTATTTGCTGGTCAAGGTGCCAGTATCTAGGGATGGGACGGGATTTCTATG  
 ATCAGTATCCGATTGTTAAAGAAACGATTGATCGAGCGAGTCAGGTGCTAGGTTATGATTTGCGTTATGT  
 CATCGATACGGAAGAAGACAAACTCAATCAGACCCGCTATACGCAACCCAGCCATTCTAGCGACTTCGGTT  
 CCTATCTACCGTTTATTGCAAGAAAAGGGGTATCAGCCTGATATGGTTGCTGGTTTGTCTCTTGGAGAATA  
 CTCTGCCCTTGGTGGCAAGCGCGCCTTGGATTTTGAAGATGCGGTTGCTTGGTAGCTAAGCGTGGAGGC  
 TATATGGAAGAAGCGGCTCCTGCTGACTCTGGCAAGATGGTAGCAGTTCCTCAATACGCCAGTAGAGGTCA  
 TTGAAGAAGCCTGTCAAAAAGCTTCTGAACTTGGAGTGGTTACTCCAGCCAATATAACACACCTGCACA  
 AACTGTCTATTGCTGGAGAAGTGGTTGCAGTTGATCGAGCGGTGAACTTTTGAAGAAGCAGGTGCCAAA  
 CGCTTGATTCTCTTAAAGGTGTCAAGTCCCTTTCACACCTCTCTCCTTGAACCTGCTAGCCAGAACTAGC  
 TGAACCTCTGGCTCAGGTAAGTTTTCAGATTTTACTTGTCCCTAGTCGGCAATACAGAAGCTGCTGTGA  
 TGCAAAAAGAGGACATTGCTCAGCTCTTACCGCTCAGGTCAAGGAACCCGTTCTGTTTCTATGAAAGTAT  
 TGGGGTCATGGAAGAAGCAGGCATAAGCAACTTTATCGAGATTGACCCGGGAAAGTCTTGTCAAGTTT  
 GTTAAAAAATTGATCAAACTGCTCACTTAGCTCATGTGGAAGATCAAGCGAGTTTAGTAGCACTTTTAG  
 AAAAATCGAGCACCACCACCACCACCCTGA

Fig 56

2CFE35 "homologue of SEQ. ID NO. 31" 35

ATCAAACTAGAACATAAAAAATATCTTATTACAGGTCGAGTCGTGGAAATGGTCTTGCCATGCCCCA  
 AGTTTGTCAAGCAGGAGCCAACTTGTCTTAAACAGTCGTGGGCAATCTCAGAAGAATTGCTGGCTCA  
 GTTTTCAAACTATGGTATCAAGGTGGTTCCTCAATTCAGGAGATGTATCAGATTTTGCAGACCTTAAGCGT  
 ATGATTGATCAAGCTATTGCAGAACTGGGTTCAGTAGATTTTGGTCAAGAAATGCAGGCAATACCCAAAG  
 ATACTCTATGCTCAAGATGACAGAAGCAGATTTTGAAGAAAGTCTCAAGGTCAATCTGACTGCTGGCTT  
 TATATACACAATCAGTCTTGAACCGATGATGAAGCCOAGAGAAGGTGCTATCATTAATATGCTTAGT  
 GTTGTGCTTTTATGGGGAATATTGGTCAAGCTAACTATGCTGCTTCAAGGCTGGCTTGAATGGCTTTAC  
 CAAGTCTGTGGCAGCGAGGTCCTAGTCCGAATAATACGAGTCAATGTGATTGCTCCAGGAATGATTGAG  
 TCTGATATGACAGCTATCTTATCAGATAAAGATTAAAGGAAGCTACACTAGCTCAGATTCCGATGAAAGAA  
 TTGGGCAGGCAGAGCAGGTTCAGATTTGACAGTATTTTAGCAGGGCAAGATTATCTAACTGGTCAAGT  
 GATTGCCATTGATGGTGGCTTAAGTATGCTCGAGCACCACCACCACCACCCTGA

Fig 57

2CFE36 "homologue of SEQ. ID NO. 32"

ATCGGAGTGAAAAAGAACTAAAGTTGACTAGTTTGTAGGACTGTCTCTGTTAATCATGACAGCCTGTG  
 CGACTAAATGGGTTAACTAGCGATATTACAGCCGAATCGGCTGATTTTGGAGTAAATTTGGTTTACTTCTTT  
 GCGGAAATCATTCGCTTTTATCGTTTGAATATTAGTATCGGAGTGGGGAATTATCTCTTTACGGTCTTGAAT  
 COTACAGTCTCTTGCCAGTCTTTCAGGTGCAAAATGGTGGCTTCTAGGAAAATGEAGGAAGCTCAGCCAG  
 GCAITTAAGGCGCTTCGAGAACAATATCCAGGTGAGATATGGAAAGCAGAACCAAACTAGAGCAGGAA  
 TGCGTAAAGTAATTAAGAAGAAATGGGTGTGACAGCTCAGACTCTCTTGGCCGATTTTGAATCAGATGGC  
 GGTTATTTGGCCCTGTTCCAAGCCCTATCAAGAGTTGACTTTTAAAGACAGGTCAATTTCTTATGGAATTA  
 ACCTTGGTAGTGTGATACAACCTTGTCTCCGATTTTAGCAGCAGTATTCACCTTTTAAAGTATTTGG  
 TTGTTCAACAAAGCTTTGTCTGAGCGAAATGGCGCTACGACTGCGATGATGATGGGATTCCAGTCTTGA  
 TTTTATCTTTGACAGTTTATGCGCCAGGTGGAGTGCCTTACTGGACAGTGTCTAATGCTTATCAAGTC

(cont'd)  
Fig 57

2 CFE 36

TTGCCAAACCTATTTCTTGAATAATCCATTCAAGATTATCGCAGAGCGCGAGGCCGTAOTACAGGCACAAA  
AAGATTGGAAAAATAGAAAAAGAAAGCCAAGAAAAAGGCTCAGAAAAACGAAACTCGAGCACCACCAC  
CACCACCACTGA

2 CFE37 "homologue of SEQ. ID NO. 33"

ATGAADATTAGTAAAGGGCACTTATTAAATTATCCATCTTGATTCCCTACTTGCTTTTATCTATTTTGGGC  
TTGATGTGGTCTATTTCGACCAACAGTGCTATTTTAATTGAAGAAGGCAAGAGCGCCTTGCAGTTGGTTCG  
AAACCAAGGAATCTTTTGGATTGGTAGTTTGATACTGATTGCCCTTAATTTATAAATTGAGACTAGATTTT  
TGAGAAATGAGCGACTAATCATTTTATTTATTAATAGAAATGCTTTTATTGTTCTTGGCTCGTTTTATT  
GOTATTCAGTAAACGGGGCATACGGTTGGATTTCGGTTGCAGGAGTAACTATTTCAGCCAGCTGAGTACT  
TAAAAATCAATTATTATTGGTATTTAGCTCACCAGATTCTCCAAACAGCAAGAAGAAATAGCTACTTATGA  
TTTTCAAGTTTGTACTCAAAATCAATGGCTTCCCCGTGCTTTAATGATTGGCGATTGCTTCTCTAGTTCT  
GATTGGAATTTGGGAATTTCCCTGATTTAGGAAATCGGACTATTTTAGTCTTGGTTTCTTGGATTATGT  
ATACAGTTAGTGGAAATCGCTTATCGCTGTTTCAACCACTTCTGGCGCTCGTATCTGCCGCTTCTGTCTTGO  
TGTGACCACTATCAGCCTAATCGGTGTTGAGACCTTTTCAAAAAATTCAGTATTTGGCTATGTAGCCAAA  
CCCTTAGTGCTTTTAAATCTTTTGGCGATCGTGCTGATGCAGGTCACCAGTTAGCTAATTTCTTATTTT  
GCCATGCTCAATGGTGGTTGGTTGGTCTAGGTCTTGGAAACTCGATTGAAAAACGAGGTTATTTGCCAG  
AAGCTCATACAGACTTTGTCTTTTCTATCGTGATTGAAGAAATTTGGCTTTGTGGTGCCAGTCTTATTTAG  
CTCTCTGTTTTTCATGATTTTGGGATTATCTTGGTGGTATTTCGAGCGGAGAAATCTTTCAATGCCATGG  
TTGCATCCGTGTGCGAGGGAATGATTTGGTTGAGGTTATTTGTCAATATCGGAGGGAATTTGGGCTTGATT  
CCATCTACAGGAGTAACCTTCCCTTCTTATCCAGGGTGGAATAGTCTTCTAGTCTTATCAGTGCGAGT  
ACCTTTGTCTTAAATATTGATGCCAGTGAAAAACGGCGCTAAGTTGTACCGAGAAATGGAAAAATCAACCA  
ATGAACCTTCTGTGGAAGCTCGAGCACCACCACCACCAGTGA

Fig 58

2 CFE38 "homologue of SEQ. ID NO. 34"

ATGCTCGCAATTTTAACCTTTATCTGGTTTTCGGGAATTATTGTAGTGGTGACGAGTTCGGGCACTTCTA  
CTTTGCCAAGAAATCAGGGATTTTAGTACGTGAATTTGCCATCGGTATGGGACCTAAAAATTTTGTCTACA  
TTGCCAAGGATGGAAACGGCCTATACCATTCGAATCTTGCTCTGGGTGGCTATGTCCGCATGGCCGGTTG  
GGGTGATGATACAACTGAAATCAAGACAGGAACGGCTGTAGTTTGACACTTGCTGATGATGGTAAGGTT  
AAAGGATCAATCTCTCAGGTAAAAATTTGGATCAAAACAGCCCTCCCTATGCAGGTGACTCAGTTTGATT  
TTGAAGCAAGCTCTTTATCAAAAGGATTGGTTCTGGAAAGAAAGAAATTTGCAGTGGATCAGGATGC  
AAGGTTGTGGAAGCAGATGGTACTGAGGTTCCGATTGCACCTTTAGATGTTCAATATCAAAATGCGAAT  
ATCTGGGCAAACTGATTACCAATTTTGCAGGTCTATGAACAATTTTATCTTAGGTGTCTGTTTGT  
GGTTTAAATCTTTATGCAGGGTGGTGTGAGAGATGTTGATACCAATCAGTTCCATATCATGCCCAAGGTO  
CCTTGGCAGGTTAGGAGTACCAGAAACGGCACAATAACCAAGATTGGCTCACATGAGGTTAGCAACT  
GGGAAAGCTTGATCCAAGCTGTGGAACAAGAAACCAAGATAAGACGGCAACGACTTTGGATGTGAETA  
TTCTGAAAGGGGAGTGACAAACAAGTCACTGTACACCCGAAGATAGTCAAGGTTACCTTCTTAGG  
TGTCAACCGGGGTTAAGTCAAGATTTTCTATCCATGTTTGTAGGTGGTTTACAACTGCTGCTGACTCAO  
CTCTCCGAATCTCTCAGCTCTGAAAAATGTGATTTTCCAACCGGATTGAAACAAGTTGGGTGGAOCTGTT  
GCTATCTTAAAGGCAAGTAGTGATGCTGCTAAAAATGGAATTGAGAATATCTTGTACTTCTTGGCAATGA  
TTTCCATCAATATTGGGATTTTAAATCTTATTCGATTCCAGCCTTGGATGGTGGTAAGATTGTGCTCAAT  
ATCTAGAAAGCATCCGCCGCAACCAATGAAACAAGAAATGAAACCTATGTCACTTGGCCGGAGTG  
GTGATCTAGGTGTCTTGTATGATTGCTGTGACTTGGAAATGACATTATGCGACTCTTTTTTAACTCGAGCA  
CCACCACCACTGA

Fig 59

2 CFE39 "homologue of SEQ. ID NO. 35"

ATGTACCATATTTAAAAAGGAATCATTACCAAAATTAAGTCCAAATACATTGTTCTTGAACCAATGGTA  
TTGGTTATATCGTGCATGTGGCAATCCTTATGCCTATTTCAGGTCAGGTTAATCAGGAGGCTCAGATTTAT  
GTGCATCAGGTTGTGCGTGAGGACGCCATTTGCTTTATGGATTTCGCTCAGAGGATGAGAAAAAGCTCT  
TTCTTAGTCTAATTTGGTCTCTGGGATTGGTCTGTATCAGCTCTTGTCTATTATCGCTGCTGATGACAAAT  
CTGGCTTGGTTCAAGCCATTGAAACCAAGAACATTACCTACTTGACCAAGTTCCCTAAAAATGGCAAGAA  
AACAGCCAGGAGATGGTGTGCTGGAAGGCAAGGATAGTAGTTGCAGGAGATGGCTTCCCTGCCAA  
GGTGGCAGTGCAAGCAAGTGCTGAAAAACCAAGAAATGGAAGGAGCTATGGAAGCCATGTTGGCTCTGGG  
CTAAGGCAACAGAGCTCAAGAAATCAAGAAATCTTTGAAGGAACGACAGATACAGCTGAGAACTA  
TATCAAGTGGGCCCTTAAATGTTGGTCAAACTCGAGCAACCAACCAACCACTGA

Fig 60

## 2 CFE40 "homologue of SEQ. ID NO. 36"

ATGAAGAAATATCGTATTTTAGCACTTCTGGAAATGATATTTTATGTGGTGGTGGACTGTCAGCTGATT  
 GGCTACCTATACCTTGAACGGCTTGCATGGGTTTGTAGCAGTGACTTGTGACAGCCTTGACAGAAAAA  
 GGATTGAAGTCTTCCAACTGATGATACCATTTTCAACATGAATTAGATAGCTTGGCTGATGTGGAATT  
 TGGGGAAATTAAGATTGGTCTTCTCCCTACTGTCACTGTGGCTGAGAAGGCCTTGOACTTTATCAAAACA  
 CCCCCAGGACTACCTGTGGTGTGGATCCTGTCTTGGTCTGCAAGGAAACGCATGATGTAGCTOTCAGT  
 TATTATCCGTTCAGGAAATTAACCTTGGAAACATGAAAACTGCAGCGCAGAAATTGCATGATTTAG  
 GAGCCGACGAGTCATTATCAAGGGAGGCAATCGTCTTAGTCAGGACAAGGCTGTGGATGTCTTTATGA  
 TGGACAGACCTTTACTATCCTAGAAATCCAGTTATCCAAGGCCAAAATGCTGGTGCAGGTTGTACCTTT  
 GGCTCTAGCAATTGCCAGTCACTTGATTAAAGGTGATAAACTTTTGGCAGCAGTAGAAAGCTCTAAGGCTT  
 TCGTTTATCGTCTATTGCACAAGCAGATCAGTATGGAGTAAGACAATATGAAGCAAAACAAAAACAACC  
 TCGAGCAACCAACCAACCACTGA

## 2 CFE41 "homologue of SEQ. ID NO. 37"

ATGATTGAANCGGAGAAAAAAGAGGAGCGAGTCTGTGATTGGTGTGGAATTGCAGGGTATGACAGT  
 TTGACCTCTGCATGGAAGAATTGGCTAGTTTAGCGAAAACGGCAGGGGAGTGGTTGTAGATAGCTACA  
 GACAAAAACGTGAAAAATATGATTCCAAGACCTTCGTGGCTCTGGTAAGTTGGAAGAGATTGCGCTTAT  
 GGTGGATGCAAGAAATCACTACTGTGATCGTCAACACCGTCTGACCCCAAGGCAGATGTCAATCTA  
 CAGGAAGTTCTCGGTGTTAAGGTCATTGACCGTATGCAGTTGATTTTGGATATCTTTGCCATGCGGGCTG  
 AAGCCATGAAGGGAAGCTCCAAGTCCACCTAGCCCAACTCAAATACCTCTTGCCTCGCTTGGTGGTCAO  
 GGGATTATGCTCAGCCGTCAAGCAGGGGAAATTGGTTCCCGTGGTCTGGTGAAAGCCAACTGGAGCTO  
 AACCGTCTGATCGTTCCCAATCAAATCACGGATATCGAGCGCCAGCTTAAGGTGGTTGAGAAAAATCGT  
 GCGACTGTCAAGAAAAACGTTTGGAGTCTAGCACTTTAAGATTGGTTTGGTTTACTAATGCTO  
 GAAAAATCAACTATCATGAACATCTTGACCAAGTAAGACCCAGTATGAAGCAGATGAGCTCTTTGCCACTCT  
 GGATGCGACAACCAAGAGTATTCATCTGGGAGGCAACCTCCAAGTAACTTTGACAGATACCGTTGGCTTT  
 ATCCAATATTGCCGACAGATTGGTGTCCAGTTTCAAGTCAACCTTGGAAAGAAAGCAAGCATGTGGACC  
 TTCTGGTTCATGTTATCGATGCTAGCAATCCTTACCACGAGGAGCATGAAAAACGGTTCTCTCCATCATG  
 AAGAGCTGGACATGGAAGTATTCCTCACTTGACGCTTTATAATAAAGCGGATTTGGTGGAGGATTTC  
 CGCTTACCAAGCCATATACCTCATTTCTGCGCAAGTGTGAGGACAGTCTGTGAAAACTTGAAGCATT  
 ATTGCTAGATAAGATTAAGGAAATTTTGAAGCATTACCTGCGAGTGCCTTTTTCAAAGTCTTACAG  
 ATTCAATGATTAGAGAGTGTGCAATTCTGGAAGAACGTGATTATCAAGAAACGGCGAAGTATTACAG  
 GGTACATTTCCGAGAAAAATAAATGAGGTTAAGAAATTTTATGACCTCGAGCACCACCACCACCA  
 CTGA

## 2 CFE42 "homologue of SEQ. ID NO. 38"

ATGGCAAAAAACATATCCTATGACCCTTGAGGAAAAGGAGAAAATTGAAAAAGAAATTAAGAAATTO  
 AAATTGGTTGCTCGACCAGAAAGTGGTAGAACGCAATTAAGATTGCCCGTTTCATACGGTGATCTTTCAAGAA  
 ACAGTGAATAAGAGCAGCTAAGGATGAACAAGCCTTTGTGCAAGGACAAATCTTAGCTTAGAAACAA  
 AAATCCGCTATGCTGAAATCGTCAATAGCGACGAGTTGCCAGGACGAAAGTAGCGATTGGTAAAAACA  
 TCACTATCCAAGAAATTTGGTGAGGACGAAAGAAAGTTTATATTATCGTAGGTTACGCTGGTGGATGC  
 CTTTGCAGGTAAGGTTTCAAATGAAAGGCCAAATTGGGCAGGCTTGATTGGCAAGAAAAACAGGTGACAC  
 AGCAACCATTOAAAACGCTGTTGGTAGCTATGATGTAATAAATCTTGAAGGTTGAAAAAACAGCCCTCGA  
 GCACCACCAACCACTGA

## 2 CFE43 "homologue of SEQ. ID NO. 39"

ATGACCAAAATTACTTGTAGGCTTGGGAAATCCAGGGGATAAAATATTTTGAAACAAAACAAATGTTGGT  
 TTAGTTTATTCATCAACTAGCGAAGAAAAACAGATGTCACTTTTACACACGATAAGATATTTCAAGCTGA  
 CCTAGCATCTTTTCTTAAATGGAGAAAAAATTTATCTGGTTAAACCAACGACCTTTATGAATGAAAGT  
 GGAAAAACAGTTTATGCTTTTAACTTACTATGGTTTGGATATTGACGATTTACTTATCATTTACGATGA  
 TCTTGACATGGAAGTTGGGAAAAATTCGTTAAGAGCAAAAGGCTCAGCAGGTGGTCATAATGATCAA  
 GTCATTATTCAACATATAGGAACTCAGGTCTTTAACCGTGTAAAGATTGGAATTGGAAGACCTAAAAAT  
 GGTATGTCAGTTTGTTCATCATGTTGAGTAAAGTTGACAGGGATGATTATATCGGTATTTTACAGTCTAT  
 TGACAAAGTTGACGATTCTGTAAACTAGTATTTTACAAGAGAAAAAATTTGAGAAAAACAATGCAGAGGTA  
 TAACGGACTCGAGCAGCACCACCACCACCACTGA

## 2 CFE44 "homologue of SEQ. ID NO. 40"

ATGATT TAAATTACAGGGGCAAATGGCCAATTAGGAACGGAACCTTCGCTATTTATTGGATGAACGTAATG  
AAGAATACGTGGCAGTAGATGTGGCTGAGATGGACATTACCGATGCAGAAATGGTTGAGAAAGTTTTTG  
AAGAGGTGAACCGACTTTAGTCTACCACTGTGCAGCCTACACCGCTGTTGATGCAOCAGAGGATGAAG  
GAAAAGAGTTGGACTTCGCCATCAATGTGACGGGGACAAAAAATGTCGCAAAAGCATCTGAAAAGCATG  
GTGCAACTCTAGTTTATATTTCTACGGAATATGTCTTTGACGGTAAGAAACCAAGTTGGACAAGAGTGGGA  
AGTTGATGACCCAGCAGATCCACAGACAGAAATATGGACGCACTAAGCGTATGGGGGAAGAGTTAGTTGA  
GAAGCATGTGTCTAATTTCTATATTTATCCGTACTGCCTGGGTATTTGGAAATTATGGCAAAACTTCGTTT  
TTACCATGCAAAATCTTGGCAAACTCATAAGACTTTAACAGTTGTAAATGACCAGTACGGTCGTCCGAC  
TTGGACTCGTACCTTGGCTGAGTTCACTACCTACCTGAGTGAATAAGGAATTTGGTTATTATCATT  
TGTOAATGATGGCAGACAGAAGACACAACATGGTATGATTTTGCAGTTGAAATTTGAAAGATACAGATGT  
CGAAGTCAAGCCAGTAGATTCCAGTCAATTTCCAGCCAAAGCTAAACGTCCGCTAAACTCAACGATGAGC  
GTGGCCAAAGCCAAAGCTACTGGATTGTATTCCAACCTTGGCAAGATGCATTGCAAGAATTTTACAAAC  
AAGAAATGAGACTCGAGCACCACCACCACCACCTGA

## 2 CFE45 "homologue of SEQ. ID NO. 41"

ATGAAACGTTCTCTCGACTCTAGAGTCGATTATAGTTTGCTCTTGCCAGTATTTTTCTACTGGTCATCGGT  
GTGGTGCTATCTATAGCCGTTAGTCATGATTATCCCAATAATATTCTGCCCATTTTAGGGCAGCAGGT  
CGCGTGATTGGCTTGGGGCTTGTGATTGGTTTTGTGGTCATGCTCTTAATACAGAATTTCTTTGGAAGG  
TGACCCCTTTCTATATATTTAGGCTTGGGACTTATGATCTTGCCGATTGTATTTATAATCCAAGCTTAG  
TTGCATCAACGGGTGCCAAAACTGGGTATCAATAAATGGAATTACCCTATTTCAACCGTCAGAATTTAT  
GAAGATATCCTATATCCTCATGTGGCTCGTGTCTTTGTCCAAATTACAAAGAAACATAAGGAATGGAGA  
CGCACGGTTCCGCTGGACTTTTTGTAAATTTCTGGATGATTTCTTTACCATTCCAGTCTAGTTCTTTTA  
GCACTTCAAAATGACTTGGGACGGCTTTGGTTTTGTAGCCATTTTCTCAGGAATCGTTTTATTATCAGG  
GGTTTTTGAAAAATTATTATCCAGTATTTGTGACTGCTGTAAACAGGAGTTGCTGGTTTTCTTAGCTATCT  
TTATTAGCAAGGACGGACGAGCTTTTCTTACCAGATTGGAATGCCGACCTACCAATCAATCGGATTTT  
GGCTTGCTCAATCCCTTTGAGTTTGCCCAACAACGACTTACCAGCAGGCTCAAGGGCAGATTGCCATT  
GGGAOTGGTGGCTTATTTGTGAGGGATTTAATGCTTCGAATCTGCTTATCCCAGTTCCGAGATCAGATAT  
GATTTTACGGTTATTGCAAGAGATTTTGGCTTATTTGGCTCTGTCTGGTTATTGCCCTCTATCTCATGTT  
GATTTACCGTATGTTGAAGATTACTCTTAAATCAAAATAACCAGTTCTACACTTATATTTCCACAGGTTTGA  
TTATGATGTTGCTCTTCCACATCTTTGAGAATATCGGTGCTGTGACTGGACTACTTCTTTGACGGGGATT  
CCCTTGCTTTTCTTTGCAAGGGGGATCAGTATTTCAAGTAATCTGATTTGGTGTGGTTTTGCTTTTATCG  
ATGATTTACAGACTAATCTAGCTGAAGAAAAAGAGCGGAAAGTCCATTCAAACGGAAAAAGGTTGTA  
TTAAAACAAATTAACCTCGAGCACCACCACCACCACCTGA

## 2 CFE46 "homologue of SEQ. ID NO. 42"

ATGGGAAAAATCATCGGAATCACTGGGGGAATGCTCAGGTAAGTCAACTGTGACAAAATTTTCTAAGAC  
AGCAAGCTTTCAAGCAGTGGATGCCGACGCACTGCTCCACCACTACAGAAAACCTGGTGGTCTGTT  
TGAGGCTTAGTACAGCACTTTGGCAAGAAATCAATCTTGAAAAACGGAGAACTCAATCGCCCTCTCTTA  
GCTAGTCTCATCTTTTCAAAATCTGAAGAGCAAAAAATGGTCTAATCAAAATCAAGGGGAGATTATCCGTG  
AGGAACCTGGCTACTTTGAGAGAACAGTTGGCTCAGACAGAAGAGATTTTCTTCATGGATATTTCCCTACT  
TTTGTAGCAGGACTACAGCGATTGGTTTGTGAGACTTGGTTGGTCTATGTGGACCGAGATGCCCAAGTA  
GAACGCTTAATGAAAAGGGACCAAGTTGTCCAAAGATGAAGCTGAGTCTCGTCTGGCAGCCCAAGTGGCCT  
TACAAAAAAGAAAGATTGGCCAGCCAGGTTCTTGATAATAATGGCAATCAGAACCAGGTTCTTAATC  
AACTGCATATCTTCTTGAGGQAGGTAGGCAAGATGACAGAGATCTCGAGCACCACCACCACCACCT  
GA

## 2 CFE47 "homologue of SEQ. ID NO. 43"

ATGAGAAAAATTTATCAATGGTGGATTACCACTGCAAGGTGAAATCACTATTAGTGGTGCTAAAAATA  
GTGTCGTTGCCCTAATTCAGCTATTATCTTGGCTGATGATGTGGTGACTTTGGATTGCGTTCCAGATATT  
CGGATGTAGCCAGTCTTGTGCAAAATCATGGAATTGATGGGAGCTACTGTTAAGCGTTATGACGATOTATT  
GGAATTTGACCAAGAGGTGTTCAAAATATTTCAATGCGCTTATGGTAAAAATTAACAGTCTTCGTGCATCT  
TACTATTTTATGGGAGCCTCTTAGGCGTTTTGTGAAAGCGACAGTTGGTCTACCGGGAGGATGTGATCT  
TGGTCTCTGCGATTGACTTACACCTAAGGCGTTTGAAGCTATGGGTGCCACTGCTAGCTACGAGGGA  
GATAACATGAAGTTATCTGCTAAAGATACAGGACTTCAATGGTGCAAGTATTTACATGGATACGGTTAGTG  
TGGGAGCAACGATTAATACGATGATTGCTGCGGTTAAAGCAAATGGTCTGACTATTATTGAAAAATGCAGC

2 CFE 47 (contd)

Fig 68 (contd)

CCGTGAACCTGAGATTATTGATGTAGCTACTCTCTTGAATAATATGGGTGCCCATATCCGTGGGGCAGGA  
 ACTAATATCATCATTATTGATGGTGTGAAAGATTACATGGGACACGTCATCAGGTGATTCCAGACCGCA  
 TTGAAGCTGGAACATATATCTTTAGCTGCTGCAGTTGGTAAAGGAATTCGTATAAATAATGTTCTTTAC  
 GAACAECTGGAAGGGTTTGTGCTAAGTTGGAAGAAATGGGAGTGAGAAATGACTGTATCTGAAGACAGC  
 ATTTTGTGCGAGGAACAGTCTAATTTGAAAGCAATCAATATTAAGACAGCTCCTTACCCAGGCTTTGCAA  
 CTGATTGCAACAACCGCTTACCCCTCTTTACTAAGAGCGAATGGTCTGGTACAATTGTGCTACGATT  
 TACGAATAACCGTGTAATCATGTTTTGAACTAGCAAAGATGGATGCGGATATTTGACAACAAATGGTC  
 ATATTTGTACACGGGTGGACGTGATTIACGTGGGGCCAGTGTAAAGCGACCGACTTAAGAGCTGGGGC  
 TGCCTACTGTATTGCTGGGCTTATGGCTGAAGGCAAACTGAAATTACCAATATCGAGTTTATCTTACGT  
 GGTATTCTGATATTATCGAAAAATTACGTAATTTAGGAGCGGATATTAGACTTGTGAGGATCTCGAGC  
 ACCACCAACCACTGA

2 CFE48 "homologue of SEQ. ID NO. 44"

Fig 69

ATGTCAAGAAATTGAATTTTCACCATCTTTGATGACCATGGATTGACAAAATTCAAAGAGCAGATTACTTT  
 TTGAATGATAAAGTAGCATCTTATCATATCGATATTATGGATGGCCATTTTGTTCCTCAATATTACCTTGT  
 CTCTTGGTTTCAATCAAGAGTTCAAAAAATTAGTGACACACCTTTATCAGTTTCTGATGGTCACAGAC  
 CCAACCTTTTGGGTAGATCAAGTTCTCGATTACAATGTGAGTATATTTGTATTCTGCTGAAGTTCTGAA  
 TGGTCTTGTCTTTCTGTTTGAATTGATAAAATTCATGATGCAGGTCTAAAGGCTGGTGTGCTTAACTCTG  
 AAACAACCTGTTTCTACAATCTTTCCTACATTGATTTACTTTGACAAAAGTAACCTATTATGACTGTAGATCCA  
 GCTTTTGCAGGACAACGCTTTTGGAGTCTACCTTGTATAAAATCCAAGAACTCCATCAGCTTAGAGTTCA  
 GAATGCTTATCACTACATCATTGAGATGGATGGTTCTTCGAGTCGTAAGACTTTCAAACAAATTGATGTG  
 GCAGGACCAAGATATTTATGTTATAGGTCGCAGTGGATTATTTGGTTTGGATGACGATATTGCCAAAGCCT  
 GCGATATCTGTTCTAGAGATTACGAAGAAATGACCGGAAAAACAATGCCAATCAAACCTCGAGCACCAACC  
 ACCACCACTGA

2 CFE49 "homologue of SEQ. ID NO. 45"

Fig 70

ATGAGAAATATGGCTTTGACAGCAGGTATCGTTGGTTTGCCAAACGTTGGTAAATCAACACTATTTAATG  
 CAATTAACAAAGCAGGAGCAGAGGCAGCAAACTACCCATTTGCGACTATTGATCCAAATGTTGGAATGG  
 TGAAGCTCCAGATGAACGCCTACAAAACTAACTGAAATGATAACTCCTAAAAAGACAGTTCCACAA  
 CATTTGAATTTACAGATATTGCAAGGATTTGTAAGGAGCTTCAAAAGGAGAAGGGCTAGGGAATAAAT  
 TCTTGGCCAAATATTCGTGAAGTAGATGCGATTGTTACGTTAGTTCTGCTTTTGAATGATGAAAAATGTAATG  
 CGCGAGCAAGGACGTGAAGACGCTTTGTAGATCCACTTGCAGATATTGATACAATTAATCTGGAATTAA  
 TTCTTGGTGAATTAAGATCAGTGAACAAACGATATGCGCGTGTAGAAAAATGACACGTACGCAAAAAAG  
 ATAAAGAAATCAGTAGCAGAAATCAATGTTCTTCAAAAGATTAAACCAGTCTTAGAAGACGGGAAATCAG  
 CTGCTACCATTTGAATTAACAGATGAGGAACAAAGGTTGTCAAAAGGTTCTTTCTTTTGACGACTAAACC  
 AGTTCTTATGTAGCTAATGTGGACGAGGATGTGGTTTTCAGAACCTGACTCTATCGACTATGTCAAACAA  
 ATTCTGTAATTTTGCAGCGACAGAAAAATGCTGAAGTACTGTTATTTCTGCGCGTGTGAGGAAGAAATTT  
 CTGAATTTGATGATGAAGATAAAAAAGAGTTTCTTGAAGCCATTGGTTTGACAGAATCAGGTGTAGATAA  
 GTTGACGCGTGCAGCTTACCACTTGTCTTGGATTGGGAACCTTACTTACAGCTGTGTAAAAAGAAAGTTCCG  
 GCTTGGACTTTCAAACGTTGATGAAGGCTCCTCAAGCAGCTGGTATTATCCACTCAGACTTTGAAAAAG  
 GCTTTATTCGTGCAATACCATGTCTATGAAGATCTAGTGAAATATGGATCTGAAAAGGCGGTAAAGAA  
 AGCTGGACGCTTGGGTGAAGAAAGAAATATATCGTTCAAGATGGCGATATCATGGAAATTCGCTTT  
 AATGTCCTCGAGCACCAACCACTGA

2 CFE50 "homologue of SEQ. ID NO. 46"

Fig 71

ATCGAAATCGAAAAAACCAATCGTATGAATGCGCTCTTTGAATTTTATGCGGGGCTTTTGACAGATAAGC  
 AAATGAATTTATCGAGCTCTACTACGCTGATGATTACAGCCTTGCTGAAATTTCCGAGGAGTTCCGTGT  
 CACTGTCAGGCTGCTATGACAATATCAAGCGAACAGAAAAAGATTCTGGAAGATTATGAGATGAAATTT  
 GCACATGACTCGGACTATATTGTCCGCACTCAGATTTTGTATCAGATTTTGGAGCGCTATCCCAAGGATA  
 ACTTCTGCAAGGACAGATAGAAATTTTAAACAGCATTGATAATAGAGAATCTGAGCACCAACCACTGA  
 ACCACTGA

2 CFE51 "homologue of SEQ. ID NO. 47"

Fig 72

ATGACCTTAGAATGGGAAGAAATTTCTAGATCCTTACATTCAAGCTGTTGGTGAAGTTAAAGATTAACTTC  
 GTGTATTCTGTAAGCAATATCGTAAGCAAAATAAGCATTCTCCAATTTGAGTTTGTGACCGGTCGAGTCAA  
 GCCAATTGAGAGCATCAAAGAAAAATGGCTCGTCTGTCGATTACTTATGCGACCTTGGAACAGATTG

- 2 CFE 51 (Contd.)
- Fig. 72 (Contd.)
- CAGGATATTGCTGCTTACGTGTGATGGTTTCAGTTTGTAGATGACGTCAAGGAAGTAGTGATATTTTGC  
 ACAAGCGTCAAGGATATGCGAATCATACAGGAGCGAGATTACATTACTCATAGAAAAGCATCAGGCTATC  
 GTTCCATCATGTGGTAGTAGAATATACGGTTGATACCATCAATGGAGCTAAGACTATTTTGGCAGAAAT  
 TCAAAATTCGTACTTTGGCCATGAATTTCTGGGCAACGATAGAACATTCTCTCAACTACAAGTACCAAGGG  
 GATTTCCAGATGAGATTAAGAAGCGACTGGAATTACAGCTAGAATCGCCCATCAGTTGGATGAAGAA  
 ATGGGTGAAATTCGTGATGATATCCAAGAAGCCAGGCACTTTTGATCCTTTGAGTAGAAAATTAATG  
 ACGGTGTAGGAAAACAGTGACGATACAGATGAAGAATACAGGCTCGAGCACCACCACCACCACCTGA
- 2 CFE 52 "homologue of SEQ. ID NO. 48"
- ATGGAACCTTAATACACACAATGCTGAAATCTTGCTCAGTGCAGCTAATAAGTCCCACTATCCGAGGATG  
 AACTGCCAGAGATTGCCCTAGCAGGGCGTTCAAATGTTGGTAAATCCAGCTTTATCAACACTATGTTGAA  
 CGGTAAAGAAATCTCGCCCGTACATCAGGAAAACCTGGTAAACCCAGCTCTGAACTTTTTTAACATTGAT  
 GACAAATGCGCTTTGTGGATGTGCCTGGTTATGGCTATGCTCGTGTCTTAAAAAGGAACGTGAAAAAT  
 GGGGCTGCATGATTTGAGGAGTACTTAACGACTCGGGAATCTCCGTGCGGTTGTCAGTCTAGTTGACCT  
 TCGTCATGACCCGTCAGCAGATGATGTGCAGATGTACGAATTTCTCAAGTATTATGAGATTCCAGTCATC  
 ATTGTGCGCAACCAAGGCGGACAAGATTCTCGTGGTAAATGGAACAAGCATGAATCAGCAATCAAAAAAG  
 AATTAAACTTTGACCCAAGTGACGATTTCACTCTTTTCATCTGTGCAAGGCGAGGATGGATGAGG  
 CTTGGGATGCAATCTTAGAAAAATTTGGCGGCCGCACTCGAGCACCACCACCACCACCTGA
- Fig. 73
- 1 CFE 53 "homologue of SEQ. ID NO. 49"
- ATGAAAACAAGAAAAATCCCTTTGCGCAAGTCTGTTGTGTCTAACGAAGTGATTGATAAGCGTGATTGTC  
 TCCGCAATTGTCAAGAACAAGGAAGGACAAGTCTTTATTGATCCTACGGGCAAGGCCAATGGCCCGCGCG  
 CTTATATCAAACTAGACAAATGCAGAAGCCCTAGAGGCGAAAAAGAAGAGGTCTTTAACCGCAGCTTTA  
 GCATGGAAGTGAAGAAAGCTTTTATGACGAGTTGATCGCTTATGTGGATCAAAAGTGAAAAAGAAGAG  
 AGTTGGGACTTGAACTCGAGCACCACCACCACCACCTGA
- Fig. 74
- 2 CFE 54 "homologue of SEQ. ID NO. 50"
- ATGTTAAACCCCTCTATTGATACCTTGCTCGACAAGGTTCCCTCAAAATATTCACTCGTAATCTTGGAAGC  
 AAAACCTGCCCACGAATTGGAAGCAGGTGCCCGAGCAACTCAAGGTTTCAAGTCTGAAAAATCAACTCTT  
 CGCCTTTAGAAGAAATCGAATCAGGAACCGTTACAATTCAACCAGATCCAGAAGGAAAAACGTGAAGCA  
 GTGCGTGGCGTATCGAAGAAAGAAAAACGGCGCAAGAAAGAAAGAAAAAGAAAAATCAAGAGCAAAAT  
 TGCTAAAGAAAAAGAAAGATGGTGAAAAAATTCTCGAGCACCACCACCACCACCTGA
- Fig. 75
- 2 CFE 55 "homologue of SEQ. ID NO. 51"
- ATGTCAATTAACATCAAAAACAACGTGCTTCTCAACAGCCAGGCCACACACCCCTCAAAOCTATCATCCAAA  
 TCGGGAATAATGGACTCAAACGACCAAAATCAAAACAGCOTCCGTCAAGCTCTTGATCGCGCTGAATTA  
 TCAAGGTTACTCTCTTACAAAAACAGATGAAAAATCCACGAAGTAGCTGAAATTTTGAAGAAAGAAA  
 TCGGTGTTGGATACAGTCCAAAAAATAGGACGCATCTTGATTTTGTTTAAACAATCTAGCAAGAAAGAAA  
 TCCCAAGATTTCTAAGAAAGTCAAAGAAATCTCGAGCACCACCACCACCACCTGA
- Fig. 76
- 2 CFE 56 "homologue of SEQ. ID NO. 52"
- ATGGCATTGAAAAATTATATACAGATTTTGTGTGGAAGCAGTCTATGATCTGACAGTCCCAAGCCTGC  
 AGCGCGAGGGAATCAAGGCTGTTTGTGCGATTGGATAATACCCCTCATGCTTGGAAACAACCTGATGG  
 AAGGCCAGAGATGAAGCAATGGCTACATGACCTTCGGGACGCGGTATTGGCATTATCGTAGTGTCAAAT  
 AACACCAAAAAACGCTTCAACGAGCAGTTGAGAAATTTGGGATTGATTACGTTTACTGGGCCTTGAAGC  
 COTTCACATTTGGTATTGACCGTGCTATGAAGGAATTCACATGACAAAAAGGAAGTGGTCATGGTTGG  
 CGACCACTCATGACAGATATACGAGCAGCCACCGTGCAAGGATTCGGTCAATTTTAGTCAAAACCCCTG  
 GTCAAGATGACTCAATCAAAACGACGATTAACCGAACTCGTGAGCGTCTGTTATGAGAAAAATCACTG  
 AAAAGTACGGACCGATTACATATAAAAAAGGAATTCGAGCACCACCACCACCACCTGA
- Fig. 77
- 2 CFE 57 "homologue of SEQ. ID NO. 53"
- ATGTTTCAAAAAATTTTAATTGCCAATCGTGGTGAATTTGCGGTTCTGATTATCCGTGCGGCACGTGAATT  
 GGGGATTGCGACGGTAGGGTTTATTCAACTGCTGATAAGGAAGCTCTTCATACCGCTTTGGCAGATGAA  
 GCATTTTGTATTGGTCTGGCAAGGCAACAAGTCTTATCTCAATATTAATGCAAGTTCTATCAGCTGCAOT  
 CTTGACTGAGGAGAGCTATTACCCCTGGTTTGGATTCTCAGTGAAAAATTCAAAATTTGCGACCATGT
- Fig. 78



2CFE57

GTGAAGAGTAGGTATCAAAGTTTATCGGTCCATCTGGTCATGTTATGGATATGATGGGGGATAAGATCAA  
 TGCCTTGTCTCAGATGATTAAAGCAGGTGTGCCTGTTATACCAGGTTTCAAGATGGAGAAGTGCATAACTCT  
 GAAGAAGCTTTGATTGTTGCTGAAAAAATTGGCTATCCTGTTATGCTCAAGGCTTCAGCAGGTGGAGGTG  
 GTAAAGGATTCGTAAAGOTTGAAAAACCATGACCTCGTTTCTGCCTTTGAAACTGCTCTAGTGAGGC  
 CAAGGCAATTATGGCAATGGTGCCATGTACATAGAACGGGTATCTATCCAGCTCGGCACATTGAGGTT  
 CAAATCTAGOTGATGAGCATGGACATGTGATTCACCTTGGGTGAACGGGATTGTTCTCTTCAAAGGAATA  
 ACCAAAAGGTTTGAAGAAAGTCCCTCGATTGCAATCGGAAAAACGCTGCGTCATGAAATAGGTGCTG  
 CTGCTGTTCCAGCGGCAGAGTTTGTGCTATGAGAATGCAGGAACCATTTGAATTTCTTCTGATGAAGC  
 AAGTAAATAATTTCTATTTCAATGGAGATGAATACTCGTTTCAGGTAGAACATCCAGTAACAGAGTTTGT  
 TCAGGTGTTGATATCGTTAAGGAACAGATTGCAATTGCGGCAGGTGACGCTTTGTCTGTTAAGCAAGAG  
 ATATTGCTCTACGGGTCATGCCATCGAGTGTGATCAATGCAGAAAAACCGCCTTTAACTTTGCTCCA  
 AGTCCAGGTAAGATTACTAATCTCTATCTGCAAGGTGGAGTTGGCTTGCAGCGTGGATTGAGGTTT  
 ATCCAGGTTATACCATTCGCTTATTATGATAGTATGATTGCCAAAAATCATAGTACACGGCGAAAAATCG  
 TTTTACGCTTGTGAAAAATGCAACGTGCCCTCTATGAATTAGAGATTGAAGGAGTGCAGAACCAATGCA  
 GATTTCAGCTTGTATCTCATTTTCAGATCGCAATGTCAATTGCTGGGGAATTATGATACTTCTTCTGATGGA  
 AACCTTCTTACCTAAATATCAAGAAAAAGAACTCGAGCACCACCACCACCACCACTGA

Fig 78 (contd)

2CFE58: "homologue of SEQ. ID NO. 54"

ATGATTTACAAAGTTTATCAAGAAAAAAGAACGTAGCCACGCGTQAAAAACAACACGCACGCTTT  
 ACCTAGACATCGATGCCAGCTCAGAACTTGAAGGGCGTATCACTGCTCGCCAACTTGTGCAAGAAAAATCG  
 CCCAGAGTACAATATCGAGTATATCGAACTCTTGTCTGACAAATTGCTCGATTACGAAAAAGAACTGGC  
 GCCTTCGAAATTACGGAGTTCCTCGAGCACCACCACCACCACCACTGA

Fig 79

2CFE59: "homologue of SEQ. ID NO. 55"

ATGAAGBATAATATATTTAAGCATTTGAGACATCTGTGATGAGACCAGTGTGCGCGTCTTGAAAAACG  
 ACGATGAGCTCTTGTCCAATGTCAATTGCTAGTCAAAATGAGAGTCACAAACGTTTGGTGGCGTAGTGCC  
 CCAAGTAGCCAGTGTGACCATGTGAGGTCAATTACAGCCTGTATCGAGGAGGCATTGGCAQAAGCAGG  
 GATTACGAAGAGGACGTGACAGCTGTTGCGGTACCTACGGACCAAGGCTTGGTCCGAGCCTTGTAGTT  
 GGTTTGTCAOCTGCCAAGGCCCTTGTGCTGGGCTCACGGAATTCCTGATTCTGTTAATCAGATGGCTGG  
 GCACCTCATGGCAGCTCAGAGTGTGGAGCCTTGGAGTTTCCCTTGTAGCCCTTTTATGTCAGTGTGGGC  
 ACACAGAGTTGCTATGTTTCTGAGGCTGGCAATTACAAGATTGTTGGGGAGACACGAGACGATGCAAT  
 TGGGGAGGCTTATGACAAGGTGCGTGTGTCATGGGCTTGACCTATCCTGCAAGGTGCTGAGATTGACGAG  
 CTGCTCATCAAGGGCAGGATTTATGATTTCCTCCCTGTCATGATTAAAGGAAGATAATCTGGAGTTCT  
 CTTTCTAGGTTTGAATACTGCTTTATCAATCTTCAATGCAATGCGGAGCAAAAGGGAGAAAGCGTGTG  
 TAGAGAAGATTGTGTGCTTCTTCCAAGCAGCAGTTATGGACATTCTGATGGCAAAACCAAGAGGCT  
 TTGAGAAATATCCTGTTAAAAACCTAGTTGTGGCAGGTGGTGTGGCAGCCAAATAAGGTCTCAGAGAAC  
 GCTTAGCAACTGAAATCAGAGATGTCAATGTATCATTCACCTCTGCGTCTGCGGAGACAAATGCAAG  
 TATGATTGCTTATGCCAGTGTGAGCGAGTGGAAACAAAGAAACTTTGCAAACTTGGACCTCAATGCCAAA  
 CCAAGTCTTGCCTTTGATACCATGAACTCGAGCACCACCACCACCACCACTGA

Fig 80

2CFE60: "homologue of SEQ. ID NO. 56"

ATGTGTGAAATTTGTTGTTGTTGTTGAAAAACAAATGCAACTGATATTTTGATTCAAGGCTTGAAAAAGC  
 TTGAATACCGTGGCTATGATTCTGCGGGAATTTTGTCTAGATGGTGCTGATAACCATTTGGTGAAGGCT  
 GTTGTGTTATGCAAGAAATTTGCTGCCAAGACAGCTGGTGTGAGGGAACTGGTATCGACATACTC  
 GTTGGGCAACTTATGGGAAACCAACGGAAGCAATGTCTACCCACACCGCTCTGAGACAGAACGTTTG  
 TCTTGTTCACAAATGGGGTGATTGAAAACTACCTTGAAATTAAGAAAGAAATACCTTGTGGGCACCACTT  
 CAAAGGGCAAAACAGATACGGAATCGCCGTACATTTGATTGGAATAATTTGCGGAAGAAAGACGCTCTCTC  
 AATTCCTTGAAGCTTTAAAAAAGCTCTTCAATATATCCGTGGTTCAATGCTTTGCTTGTGATGACTCTG  
 AAAATCCAGATGTCATCTATGTAGCGAAAAACAAATCTCCACTTTGATTGGTCTTGGGGAAGGCTACAA  
 TATGGTCTGCTGAGATGCTATGGCTATGATTCTGTGAACCAACCAATACATGGAAATTCATGACCAAGAG  
 TTGGTAATCTGCAAGGCTGATAGCGTGGAAAGTTCAAGACTATGATGGTAACAGTCTGAAAGTGTGCTAGCT  
 ATACTGCGGAACCTTGAATTTGTGAGATATCGGTAAGGGAACCTTATCCTTACTACATGCTTAAGGAAATTA  
 TGAGCAACCAACTGTTATGCTAAACTCATTCAAGCTACACGGATGATGCTGGTCAAGTATGATGAT  
 CCTGCTATCATTAAGGCTGTTCAAGACGACACCGCATCTACATCCTTGCAGCTGGAACATCTTACCATG  
 CAGGATTGCTTCTAAGAAAAATGTTGGAAGAATTGACAGATACCAAGTTGAACTTGGCATCTCATCTOA  
 GTGGGGCTACGTTATGCCACTTCTCAGCAAGAAACCACTTTCATCTTTATCAGCCAATCTGGTGAACA

Fig 81



2 CFE 60 (contd.)

Fig 81 (contd.)

GCGGATAGTCGTCAAGTTTGGTCAAGGCTAATGAAATGGGAATTCCAAGCTTAACAGTGACAAACGTTTC  
CAGGTTCAACCCCTCTCAGTGAAAGCCAACTATACCATGCTCCTTACCGCAGGTCCTGAAATTGCGGTGGC  
ATCAACTAAAGCCTATACAGCGCAAATCGCAGCCCTTGCTTCTTGCAAAAGCAGTCGGAGAAGCAAAT  
GGTAATGCTAAAGCGCAAGCCTTTGACCTGGTTCATGAATTGTCAATCGTAGCTCAGTCTATCGAATCAA  
CTCTTTCAGAGAAAGAAACCATTTGAAGCCAAGGTTTCGTGAACCTTCTTGAAACAACTCGTAACGCCCTTTTA  
CATCGGACGTGGTCAAGATTACTACGTAGCCATGGAAGCAAGTCTCAAACTCAAAGAGATTTCTTATATC  
CAGTGTGAAGGTTTTGCGGCAGGADAACCTCAAGCACGGAACCATTTGCCTTGATTGAAGAAGGAACACCT  
GTCTTGGCTGTCTGTTCAGATCCAGTCCCTTGCCAACCACTCGTGAAATATCCAAGAGGTGGCAGCCC  
GTGGTGCTAAGGTCCTCACTATCGCAGAAGAAAATGTTGCTAAAGATACCGACGATATCGTCCCTTACGAC  
TGTACAACCTTACCTCTCACCATTTCATGTTGTCGTACCGACGCAATTGGTTGCTTACTTTGCAACCCCTCC  
ACCGTGGCCTCGATGTGGATAAACCAACGTAACTTGCCAAGTCAGTAACGGTAQAACCTCGAGCACCACC  
ACCAACCACTGA

Fig 82

2 CFE61 "homologue of SEQ. ID NO. 57"

ATGATACGTATCGAAAAATCTCAGTGCTCTCTACAAAGACACGTTGGCACTTAAGGATATTTCACTAGTGC  
TCCATGACCAACAATTACCGGCATCATTTGGTCCAACGGCGCTGGGAAATCAACACTATTAAAAAGGTAT  
GCTGGGAATTATCCCACTCAAGGTCAGGCATTCTCGATGACAAGGAAGTTAAAAATCCTTACACCGA  
ATTGCTTATGTGCAACAAAAAATCAATATCGACTACAACCTTCCCATCAAGGTCAAGGAATGCGTCTCGT  
TAGGACTATTTCCCTCTATCTCTCTTTTGAAGTTTAAAGGCTAAACATTGGAAGAAAGTGCAAGAGGC  
CCTTGAATACGTCGGCCTAGCTGACTACGCTGAACGTCAAATTAGTCAACTGTCTGGAGGTCAATTCAG  
CGGGTCTTGATTGGCAGATGTTTGTGTCAGGAAGCCGACTATATCTCTTTGGATGAACCCCTTTGCTGGGAT  
TGACTGTCTCAGTGAGGAAATCATCATGAATACGCTGAGAGATTGAAAAAAGCTGGGAAGACGGTTCT  
CATCGTTCACCACGACCTCAGCAAGATTCCCACTACTTTCGATCAAGTCTTACTTGTCAATCGAGAAGTG  
ATTGCTTTGTGTCACAAAGAAACCTTTTACCGAAACCAATCTAAAAGAAAGCTTACGGTAATCAACTCT  
TTTCAATGGAGGTGACCTACTCGAGCACCACCACCACCACCACTGA

Fig 83

2 CFE62 "homologue of SEQ. ID NO. 58"

ATGCCGAAGGAAGTGAATTTAACAGGCGAAGAAATGTGTCGCTTTAACCAAGAAATATTTAACGGAAGAG  
CATGTTTATTTTGTCCATAAGGCCCTTGGTCTATGCTGTGAAATGCCACAGTGCTCAATATCCCAAAATCAGG  
CGAGCCTATATCATTCACCCATCCAAAGTGGCAGGTATTTAGCTAAGCTAAAGCTGGATGCTGTAAACA  
GTAGCTTGTGATTCTTGCATGATGTGGTGGAAAGATACAGATGCGACTTTGGACGATTGGAAAGAGAGT  
TTGGTCTGATGTGCGGATGATTGTTGACGGAGTTACCAAGCTTGGCAAGGTCGAGTACAAATGATCGA  
GGAGCAATTAGCGGAAAAATCATCGCAAGATGCTCATGGCCATGTCTGAGGACATCCGCGTATTTTGGTC  
AACTGTCTGACCGCTTGCACAATATGCGGACCCGTGAACATCTTTCGAAAAGACAAGCAGGAGCOTATTT  
CCAAAGAAACCATGGAATCTATGCCCGGCTTGCCTCATGTTTGGGGATTTCCAGTGTCAAATGGGAATT  
AGAGAGCTTGTCTTCCGTTATCTCAATCCAACGGAGTTTACAAGATTACCCATATGATGAAGGAAAAAG  
CGCAGGAGCGTGGGCTTGGTGGATGAGGTAGTACAAAAATTAGAGGAGTATACGACAGAACGTCAC  
TTGAAGGGAAAGATTTATGGTCTGCCAAGCATATTTACTCAATTTTCCGCAAAATGCAGGACAAAGAGAA  
AACCGTTTGAGGAAATCTATGATCTGATTGCTATTCTGTTGATTTTAGATACCCAAAGTGTATTTATGCC  
ATGCTTGTGTTACGTGCATGAATTTTGAACCCGATGCCAGGTCGCTTCAAAGACTATATCGCCAACCGCA  
AGGCCAATGTTTATCAGTCTATCCATACGACTGTTTATGGACCAAAAGGGCCGATTGAATTCAGATTGG  
AACCAAGGAAATGCACGAGGTGGCTGAGTACGGGTTGCGGCTCACTGGGCTTATAAGAAAGGTATAAA  
GGGCAAGTTAACAGCAAGGAATCAGCTATTGGAATGAACTGGATCAAGGAGATGATGGAGCTCCAAGA  
CCAGGCTGATGATGCTAAGGAATTTGTGACTCTGTTAAGGAAAACTATTTGGCTGAGGAGATTTACGTT  
TTTACCCAGATGGAGGTGTCCGTTCCCTTCCCAAGATTTCAGGACCGATTGATTTTGGCTACGAAATCCA  
TACCAAGTCCGTTGAAAAAGCAACTGGTGCCAAGGTCAATGGCCGCATGTTTCCACTGACAACCAAGTT  
AAAGACAGGGGATCAGGTTGAAATTTATCCCAACCCGAACTCCTTTGGACCTAGCCGTGACTGGCTCAAT  
ATGTCACAGACTAGCAAGGCGCGCAATAAGATTCCGCCAGTTCTTTAAAAACCAAGATAAGGAATTGTCT  
GTCAACAAGGTCGTTGAGATGCTGATGGCTCAGTTCCAAGAAAAATGGCTATGTGGCAAAATAAATTTATGG  
AQAAGGCCCATATGATCAAGTTCTGCAAAAGACCAAGTTACAAGACAGAAAGACTCCCTCTTTGCGGCCAT  
TGGTTTGGGAAATCGGTGCGATTACCGTCTTTAACCGTCTGACTGAAAAGGAGCGCCGTGAGGAAGAG  
CGTGCCAAGGCCAAGGCTGAGGCAAGGAGCTTGTCAAAGGTGGCGAGGTCAAGGTTGAAAAATAAAG  
AACTCTCAAGGTCAAGCATGAGGGGGGAGTGGTTATTGAAGGTGCTTCTGGTCTCCTAGTGGGATTGCT  
AAGTGTGTAAACCCGTGCCCTGGTGACGATATTGTGGCTACATTACCAAGGGTCGTGTGTGGCTATTC  
ACCGTGTGACTGTATGAACCTGCGTGCCCAAGAACTACGAGCAACGCTCTCTTGTATGTGAATGGGA  
AGACCAGTACTCTAGCTCAAATAAGGAGTATATGGCCCATATCGATATCTACGGTCTCAACCGTACAGGA

2CFE62 (Contd.)

(Contd.)  
Fig 83

CTGTTGAACGATGTACTGCAAGTTCTTTCAAATACAACCAAGAATATTTCAACGGTCAATGCCAACCAA  
 CCAAGGATATGAAGTTTGCTAATATCCATGTGTCTTCGGTATTGCCAACCTCTCTACACTGACCAAGGTT  
 CTCGATAAAATTAAGATGTGCCAGAAGTTTACTCTGTCAAACGGACCAACGGCCTCGAGCACCACCACC  
 ACCAACCCTGA

2CFE64 "homologue of SEQ. ID NO. 60"

Fig 84

ATGACAGAAAGAAATCAAAAATCTGCAGGCACAGGATTATGATGCCAGTCAAATTCAGTTTTAGAGGGC  
 TTAGAAGCTGTTTCGTATGCGTCCAGGGATGTACATTGGATCAACCTCAAAAGAAGGTETTCACCATCTAG  
 TCTGGGAAATTTGTTGATAACTCAATTOACGAGGCCTTGGCAGGATTGGCCAGCCATATTCAAGTTTTATT  
 GAGCCAGATGATTCGATTACTGTTGTGGATGATGGCGGTGATATCCAGTCGATATTGAGGAAAAACAG  
 GTCGTCTCTGCTGTTGAGACCCCTCTTTACAGTCTTTCACGCTGGAGGAAAGTTTCGGCGGTGGTGGATACAA  
 GOTTTCAGGTGGTCTTTCACGGGGTGGGGTCTCAGTTGTTAATGCCCTTTCCACTCAATTAGACGTTTCATG  
 TCCATAAAAACGGTAAGATTTCATTACCAAGAATACCGTCGTGGTCAATGTTGTCGCAGATCTTGAAATAGT  
 TCGAGATACCGGATATAAACAGGAACAATCTTCACTTCACACCGGACCCAAAAATCTTCACTGAAACAAC  
 AATCTTGAATTTTGATAAAATTAATAAACGGATTCAAGAGTTGGCCTTTCTAAATCGCGGCTTCAAATTT  
 CTATCACTGATAAGCGCCAAGGTTTGAACAAACCAAGCATTATCATTATGAAGGTGGGATTGCTAGTTA  
 CGTTGATATATCAACGAGAACAAAGGATGTAATCTTTGATACACCAATCTATACAGACGGTGAGATGGAT  
 GATATCAGAGTTGAGGTAGCCATGCAATACACAACGGGTTACCATGAAAAATGTCATGAATTTCCGCAATA  
 ATATTTACACATGAAGGTGGAAACGCAAGCAAGGTTTCCGTACAGCCTTGACACGTTTATCAACGA  
 TTATGTTCTGTAAGAATAAGTTTACTGAAAGACAAATGAAGACAACTGAACAGGGGAAGATGTTTCGCGAAGG  
 CTAACTGCAAGTTATCTCAGTTAAACACCCAAATCCACAGTTTGAAGGACAAACGAAGACCAAAATTGGGA  
 AATAGCGAAGTGGTCAAGATTACCAATCGCCTCTTTCAGTGAAGCCTTCTCCGATTTCCTCATGGAAAATC  
 CACAGATTGCCAAACGTATCGTAGAAAAAGGAATTTTGGCTGCCAAGGCTCGTGTGGCTGCCAAGCGTGC  
 GCGTGAAGTCACACGTAAAAAATCTGGTTTGGAAATTTCCAACCTTCCAGGGAACTAGCAGACTGTTCT  
 TCTAATAACCTGCTGAAAACAGAACTCTTCATCGTCAAGGAGACTCAGCTGGTGGATCAGGCCAAATCTG  
 TCCGTAAACCGTGAAGTTTCAGGCTATCTTCCAAATTCGCGGTAAAGATTTTGAACGTTGAAAAAGCAAGTAT  
 GATATAAGATTCTAGCTAACGAAGAAATTCGTAGTCTTTTACAGCCATGGGAACAGGATTTGGCGCAGAA  
 TTGATGTTTCGAAAGCCCGTTACCAAAAATCTCGTTTGTATGACCGATGCCGATGTCGATGGAGCCACACA  
 TTGTAACCTTCTTTTAAACCTTGATTTATCGTTATATGAACCAATCTTAGAAGCTGGGTATGTTATATTO  
 CCAACACCAATCTATGGTGTCAAAGTTTGAAGCGAGATTAAGAATATATCEAGCCGGGTGCAATC  
 AAGAAATCAAACCTCAAAGAGCTTTAGCCCGTTATAGTGAAGGTGATACCAACCGACTATTTCAGCGTTA  
 TAAGGGCTAGGTGAAATGGACCATCATCAGCTGTGGGAAACAACCATGGATCCCGAACATCGCTTGAT  
 CGCTAGAGTTTCTGTAGATGATGCTGCAGAAAGCAATAAAATCTTTGATATGTTGATGGGGGATCGAGTA  
 GACCTCGTCGTGAGTTTATCGAAGAAAAATGCTGTCTATAGTACACTTGATGTCTCGAGCACCACCACC  
 ACCAACCCTGA

2CFE65 "homologue of SEQ. ID NO. 61"

Fig 85

ATGGGATTACTGAAGAAACAGTACGTTTTAAATTGGACGATTCCAATAAAAAAGAAATTAGCGAAACTT  
 TGACAATGTTTATGCTTCGTTGAACGATAAGGGTTACAACCCAAATTAACCAAAATCGTAGGTTACGTATT  
 GAGTGGAGACCCCTGCTACGTTCTCTGTTATAATAATGCACGAAATCAAATCCGTAAGTATGAGCGTGAT  
 GAAATCTTTGAGGAATTGGTTGCTACTATCTCAAAGGACAAGGAGTCGATCTACTCGAGCACCACCACC  
 ACCAACCCTGA

2CFE66 "homologue of SEQ. ID NO. 62"

Fig 86

ATGGTCAACTATCCACATAAAGTTTCATCACAAAAAGACAAACATCTCTTCTCAACCCAAAAATTTCCG  
 CAAATCCAGGAAATGTTCTTTGAAAAGATGATCAATGCTACCAACGACTACTATTGTTCTCAGGGCTTGGC  
 TGTATACATAAGAAACCAACTCTTATCAAAATCGTACAAAGTGGACTATCCACAACGAAGTCGTGCCAAG  
 ATTTGTAAGCCTATTTTCGACAAGCTTCAACGACGACTATTTCTGGCGTTTATAATGGATATTACATCGA  
 CTTTGAAAGTCAAGGAAACAAAAACAAACGTTGGGATTCCGATGAAAAATTTTCATCCACATCAGATTCA  
 CATATGGAACAAGTCTTGGCCAAACAAAGGAATCTGCTTTGTCCTTCTTCACTTTCTTCTCAGCAAGAAAC  
 CTACTTATTTGGCGGCAATTCGATTTGATTGCTTCTATCATCAAGATAAGGGACAAAAATCAATGCCACTTO  
 AATATATTCGAATAATATGATATGAAATCAAGGCTGGTGCCTTCCCTCAAATTCCTTATCTCAATGTTATC  
 AAAGAACATTTATTAGGTGGTAAAAACAAGACTCGAGCACCACCACCACCACCCTGA

2CFE67 "homologue of SEQ. ID NO. 63"

2 CFE 67 homologue of SEQ ID NO: 63

ATGGCTCTATTTAGTAAAAAAGATAAGTATATTGGAATCAATCCAATCGTTCGGTTAGGGAAAAACCTC  
AA3CTAAGCCAGAGGTTCCAGATGAATTATTTCCAGTGTCAGGCTGTAAGCATACCATCTATCAGAA  
GGATCTGGGAAGTGAACGTATCTGTCCGCACTGTAGCTATACCTTTCTGATTTCTGCCAAGAACGGTTGG  
CTTTGACGATTGATATGGGAACCTTCAAAGAATTGTTTACAGGGATTGAAAGCAAGGATCCCTTGCATT  
CCCTGGTTACCAAAAGAACTGGCATCTATGCGTGAAAAAACAGGTCTGCATGAAGCCGTTGTGACAGG  
AACTGCTCTTATTAAAGGTCAGACTGTGGCTCTTGGGATTATGGATTCTAATTTATCATGGCTTCTATGG  
GTACGGTTGTAGGTGAAAAAAATCACTCGTTGTTTGGATTATGCGACTGTGAAAAAATTGCCAGTTGTCT  
ATTACAACCTCTGTGGAGCCCGTATGCAGGAAGGAATCATGAGTCTCATGCAGATGGCTAAGATCTCT  
CCAGCGTTTAAACGCCATTCAAATGCTGGTCTCTTTACCTGACCATTTGACAGATCCAACCACTGGTG  
GTGTGACAGCTTCTTTCGCTATGGAAGGCGATATCATTCTGGCTGAACACAGAGCTTGGTTGGTTTGGCT  
GGCGCTCGTGTGATTGAAAAATACGGTTCGTGAAAGCTTGCCTGAGGATTTCCAAAAGGCAGAAATTCCTAT  
TAGAAATGCGCTTTGTGGATGCTATTGTCAAAAGAAGAGACTTACCAGATACGATTGCTAGCCTAGTCAG  
ATTGCATGGAGGGAGTCCCTAGACTCGAGCACCACCACCACCACCACTGA

2 CFE 68 "homologue of SEQ. ID NO. 64"

ATGAGAAATTAAGGATTGGGACGTGCGTTCAAAAACGGTAGGGGTGGCGATTAGCGATCCGCTTGGTTTTA  
CAGCTCAAGGGCTTGAATCATCCAGATAAATGAAGAACAAGGCCAATTTGGTTTTGACCGCGTTAAGG  
AATTGGTTGATACTTACAAGGTGGAACGATTGTAGTGGGCTTGCCTAAAAACATGAACAATACAAGTGG  
ACCGCGCTAGAAAGCTAGTCAAGCCTACGGAGCAAAAGCTAGAAGAGTTTTTGGTTTACAGTAGACTAT  
CAGGATGAACGCTTGACAACAGTGGCTGTGAGCGCATGTTGATTGAACAAGCAGATATCAGTCGCAAT  
AAGCGCAAGAAAGTCATTGATAAGTTAGCAGCTCAGCTGATTTTACAAAATTATTTAGATAGAAAATTC  
TCGAGCACCACCACCACCACCACTGA

2 CFE 69 "homologue of SEQ. ID NO. 65"

ATGACAAACTTACTGTAAAGACGTGACTTGAAAGGTAAAAAAGTCCTCCTTCGTGTGACTTCAACG  
TAGCATTGAAAGATGGCGTAATCACTAACGATAACCGTATCACAGCAGCTCTTCCAATTAAAGTACAT  
CATCGAACAAGGTGGACGTGCAATTCCTTTCTCTCACCTTGGACGTGTGAAAGAAGAATCTGATAAAGCT  
GGTAAATCACTTGCTCTGTAGCAGCTGACTTGGCAGCAAAACTTGGTCAAGATGTTGTTTTCCAGGTGT  
CACTCGTGGTGTGAATTGGAAGCGGCAATCAAACGCTCTTGAAGATGGACAAGTTCTCTTGGTTGAAAC  
ACTCGTTACGAAGATGTTGACGGCAAGAAAGAATCTAAAAACGATCTGAACTTGGTAAATACCTGGCA  
TCACTTGGAGATGTTCTTGTAAACGATGCACTTCGGTACAGCTCACCCTGCACAGCATCTAACCTTG  
GTATCTGACCAAAAGCTTGAAAAAGCAGTTGCTGTTCTCTTGAAGAAAGAAATTCCTACATCCAAGA  
AGCAOTTGAAACTCCAAGACGTCCATTCCTGGCTATCCTTGGTGTTCAAAAGTTTCAGACAAGATCGGT  
GTATCTGAAAACTTGTCTTGAAAAAGCTGATAAAGTCTTATCGGTGTGGGATGACTTACACATTCTACA  
AAGCACAAGGTATCGAAATCGGTAACTCACTGTAGAAGAAGACAAATTGGATGTTGGGAAAGCTCTTCT  
TGAAAAAGCAATGGTAAATTGATCTTGCAAGTTGACTCAAAAGAAGCTAACGCAATTTGCTGGTTACACT  
GAAGTGGCTGACACTGAAGGTGAAGCAGTTTCTGAAGGCTTCTTGGTCTTGACATCGGTCCAAAATCTA  
TCGCCAATTGACGAAGCTTTGACTGGTGCCAAAACAGTTGTATGGAACGGACCTATGGGTGTATTGGA  
AAACCCAGATTTCGAAGCTGGTACAATCGGTGTGATGGAACGCTATCGTGAACAACAGGAGTTAAATC  
AATCATCGGTGTGGTGACTCAGCTGCCGCAGCGAATTAACCTTGGCCGTGCAGACAAGTTCTCATGGATT  
AGTAGGGTGGTGGAGCATCAATGGAACCTCTTGGAAGGTAAAGTTCTTCCAGGACTTGCAGCCTTGACAG  
AAAAACTCGAGCACCACCACCACCACCACTGA

2 CFE 70 "homologue of SEQ. ID NO. 66"

ATGTTAAATCAGAAAAACAATCAGTTATCAAATGTTAAATGAAGAATTGCTCTTCTATTGGAAGGCG  
AAACCAATGTTTTGGCTAATCTTTCCAACGCCAATGCTCTCATAAATCAGTTTTCTTAATACCGTATTT  
GCAGGCTTTATTGTTTCGATGGAAGGAATTGGTTTTAGGCCCTTCCAAGGAGGTGTTCTCTGCATCCG  
TATTGCACTAGGCAAGGTTGTTGGTGGAGGAGCTCACTTTCAGGAAACTGTTATTGTTGGAGATGTG  
ACGAOCTATCTCAACTATATTTCTTGTGATAGTCTAGCTAAAAATGAAATTGTTGGTGGCCGATGATGAAGA  
ATGTTCACTTATTTGAGTTCTGGATCTGGATTCTTCAGAGATTGAGGATTACGATGCTATGGATCGAGA  
TTATTGGAACATTTGTCGCTATTTGCTTGAAAAAGACAACATGGGACTTTACGATGTTTGGGAAAAA  
TCTCTCGAGCACCACCACCACCACCACTGA

2 CFE 71 "homologue of SEQ. ID NO. 67"

ATGAGAAATGAACTATTGACTCGCTTTACCAAGGTAGAGTTGGAGCCAGAAATCAAGGAGAAAAAACGC  
AAACAAGTTGGGATTTAGGGGGGAATTTTAAOCCTGTTCAATGCCATCTCATTTGTTGCGOATCAAG

2 CFE 71 (Contd.)

Fig 91 (Contd.)

TACGGCAACAGTTGGGACTGGATCAAGTCTTCTCATGCGCTGAATACCAACCTCCTCACGTTGATAAAAA  
 GAAAAACCATCCCTGAACACCATCGTCTCAAGATGCTTGAGTTGGCAATTGAGGGGATTGACGGCCTAGTC  
 ATTGAACCAATTGAGTTGGAGCGCAAGGGTATTTCTACACCTACGATACCATGAAGATTTTGACAGAGA  
 AGAATCCAGATACGGATTATTACTTTATCATCGGTGCCGACATGGTTGACTATCTGGCTAAGTGGTACCG  
 AATTGATGAACTGGTTGACATGGTTTCACTTTGTGGGGGTTTCAGCGTCCACCGCTACAAGGTAAGGACTTCC  
 TATCCAGTTATCTGGGTGGACGTACCGCTCATGGATATCTCGTCCAGCATGGTGCGGGGACTTCCTTGCCCA  
 AGGTCCGAAAACCAACTTCTCTACCTCAGCCAGTGCTAGACTACATCGAGAAGGAGGGGCTTACCTC  
 GAGCATCACCACCACCACTGA

2 CFE72 "homologue of SEQ. ID NO. 68"

Fig 92

ATGAAATTTGCAAAAATAGTCAAGAGAAGCGCGTGAGCAGAGTCGCTTGACAACCTTGGACTTTGCGACA  
 GGCATTTTGATGAATTTATCCAAATTACATGGTGACCGTTCTTTTCGTGATGATGGTGACGTTGTTGGTGG  
 TATTGGTTGGCTTGGAGACCAAGCTGTAAACAGTGGTTGGTATCCAAAAAGGCAAGAGTTTGCAAGACAA  
 COTCAAACGGAATTTGGCCAAACCATCCAGAAAGCTACCGAAAGGCACTGCGGTTGATGAAAACAGGC  
 TGAGAAATTTGGCGCTCCAGTTGTGACCTTTATCAATACAGCAGGTGCTTATCCTGGTGTGGAGCGGAA  
 QAACTGGTCAAGGGGAAGCTATCGCTCCGAATCTCATGAAAATGAGTGACCTGAAAAGTTCTATTATCG  
 CCATTATATCGGTGAAGGTGGTTCAAGCGGGGCTCTGGCTCTAGCTGTCTGGGACCGGTGTCTGGATGCT  
 CGAAAAATCTATCTATGCCATTCTCAGTCCAGAAGGCTTTGCTTCCATTTTATGGAAGGACGGTACTCGCG  
 CCATGGAAGCAGCAGAACTGATGAAAACTACTTCGCATGAACTGTTAGAAATGGACGTGGTGGATAAGG  
 TGATTTCTGAAGTAGGACTTTCTAGTAAAGAACTAATTAAGAGTGTCAAAAAAGAACTCCAAACGGAGCT  
 GGCTAGACTTTCAAAAAACCGCTAGAAGAGTTGCTGGAAGAACGCTATCAACGATTTAGAAAATACCT  
 CGAGCACCACCAACCACCACTGA

2 CFE75 "homologue of SEQ. ID NO. 71"

Fig 93

ATGTCAGATAAGATTGGCTTATTCACAGGCTCATTGATCCGATGACAAATGGGCATCTGGATATCATTG  
 AACGGGCGAGCAGACTTTTGATAAGCTTTATGTGGGTATTTTTTTAAATCCCAACAACAAGGATTTCTT  
 CCTATCCGAAAATCGTAAACGGGGGCTAGAAAAGGCTTTGGACATCTGAAAAATGTTGAAGTCGTGGCT  
 TCTCATGATGAATGGTGGTCCGATGTTGCAAAAAGATTGGGTGCTACTTGTCTAGTGGTGGTTTGAGGA  
 ATGCGTCCGATTGCAATATGAAGCCAGTTTGTATTACTACAATCATCAGCTGTCTTCTGATATAAGAGCT  
 ATTATTTACATAGTCGACCTGAACATCTCTATATCAGTTTATCAGGCGTTAGAGAGCTTTGAAAGTTTG  
 TCAGGATATTGCTGCTATGTTCCCGAGAGTATTGAGGAAAGCGGCCGCACTCGAGCACCACCACCA  
 CACCACCTGA

2 CFE76 "homologue of SEQ. ID NO. 72"

Fig 94

ATGACGATTTTGTGTTGTTATCAGTGCTTCTTTCTGTATATGGTTTCTCTTAGCATGAAACCTATCAA  
 ACAGCTAAAAAGTGAAGGAGAAAAATTAGCTCAGCAGTATGCAAGATTAGAGCAGGCTGATCAGGTTGAT  
 TTATACATGCGCTTGGAACTTTATACAGCGTTCTTGGTGGTAAATAACAGCAAGAAAGCGCTTGTGTCT  
 GATTGGTAAAGATGACCATAAGATTACGTTTATCAGCTAAATCAGGGTATTTACAAGAAAAAGCAGA  
 AACGGTTCTAAGGAAAAAGGAGCTGGCAGATGACAAGATAACCTTTGGTGGTTATCAAGACAAGCC  
 AATCTGGGTAGTTAAGTCAGGATCTGATTTTATCTAGTAGATTTTGAACAGGAGCATTGGTCAACAAG  
 GAGGGCTTACTCGAGCACCACCACCACCACTGA

2 CFE78 "homologue of SEQ. ID NO. 74"

Fig 95

ATGTTGTAATCGATAAGAAAAATTCAGTTTGTAAAAAGTACGATTTTGCCCTCTGAAACTATTGATG  
 CGCAGGATATTCTTACTGGAAATCAGTGTTTAAACAATTTATGAAGAAAAATCAACTGTAGTCATGTT  
 GGGAAATCTGGTAGCCATCATTTTGATAAGTTTCATCTACCCAATGTTTTTAAAGTTTGATTTCAATGATG  
 TCAGCAAGGTAAACGACTTTAGTGTTCGTTATATCAAGCCAAATGCGGAGCATTGGTTGGTACTGACAG  
 TAAACGTAATAACGCTCTTTGACGGTGTCTGGTTCGGAGCTCGTAACTCCATCCTCATTTCTGTGATTGCOA  
 CAGTGATTAACCTGGTTATCGGTGTTTTTGTGGTGGTATTGCGGATTTTCAAAATCAGTTOACCGTGTG  
 ATGATGAAAGTTTACAACGCTATCTCAAACATCCACCTCTTTGATTGTTATTGTCTTGACTTACTCAAT  
 CCGAGCTGGATTCTGGAATCTGATTTTGGCATGAGCGTAACAACATGGAATTGGTATTGGCTTCATGATCC  
 GTGTGCAAACTTTGCGCTATCGTGACTTGGAAATACAACCTTGGCGTCAAGTACTTTGGGAACACCAACCTT  
 GAAGATTGTTGCCAAAAATATCATGCCCTCAATGGTATCTGTTATTGTGACAACCATGACTCAAAATGCTTC  
 CAAGCTTTATCTCATACGAAGCCTTCTGTCTTTCTTGGTCTTGGATTACCGATTACAGTGCCAAAGTTTG  
 GGTGTTTGAATTCGGATTATTCAAAAAAGTAAACAACCAATGCTTACTTGTCTGGAATTCCATTGACAAC

## 2 CFE 78 (Contd)

(Contd)  
Fig 95

CC TGTCTTGGTATCCTTGTCCCTTTTCGTAGTTGGTCAAAACTTAGCGGATGCTAGTGATCCACGTACAC  
ATAGACTCGAGCACCACCACCACCACCCTGA

## 2 CFE 79 "homologue of SEQ. ID NO. 75"

ATGTATAACCTATTATTAACCATTTTATTAGTATTATCTGTTGTGATTGTGATTGCAATTTTCATGCAACCA  
ACCAAAAACCAATCCAGCAATGTATTGATGCCAGTTCAGGTGATTGTTTGAACGCAGTAAAGCTCGCG  
CTTTGAGCTGTAATGCAGCGTTGACAGGGATTGTTAGTCTTTTCTGGCTAGCCATTGCCCTTAOCATTG  
ACCGTATTATCAAGTAGACTCGAGCACCACCACCACCACCCTGA

Fig 96

## 2 CFE 80 "homologue of SEQ. ID NO. 76"

ATGTTTGTAGAAAATAAATTATTTTTTGGACCACAGAAAATTTACTCTTAACCATCATCTTTTACCTATGG  
AGACAGATGGGATCTTTGATTAAACCTTTTGTAGCGTGCTTAATACAATTATGATTCCATTTTATTAGG  
GGCTCTCTTTATTATTGACAAACCTATTGTTACTTTCTTAAATAAAGTCTGTAAAGTCAATCGTTTGTCT  
TGCTATTTAAATTACCTGTGTACTTTGGTCTGGGGAATGGTCATAGGTGTTGTCTATCTCTTAOCTATTT  
GATTAAACAGTATCTAGTTTGATTATATCTAGTCAAACTATTTATAGTCGAGTACAAGACTTAATCATAG  
ACTATATTAATTATCCTGCGCTCCAGAAATTTGATGTAGAAGCTACAATTCAGCAGTTAAACTTATCCTAT  
GTTGATTTCTTCAAAATATCCTAAATAGCGTATCAAAATAGTGTGGGAGCGTCTTGTGAGCTCTTATCAG  
TACTGTTTGAATTTTGATTATGACTCCAGTTTGTGTTTATTCTTATTAGATGGACATAAAATCTTGGCC  
ATGCTTCAAAAGAACGATTCTAAAGAGGGATCGCTTGCTATTTGCAGGCTTATTAAGAATTTAAATGCCA  
CGATTGCTCGGTATATTAGTGGAGTTTCGATTGACGCAATCATTATAGGTTGTTTGGCTTATATTGGCTAT  
AGTATTATTGGTTTAAATAATGCTTTAGTTTGTGCCATTTTCTGGTGTAGCCAATTTAAATCCTTATGTG  
GGCCCAAGTATTGGTTTGATTCTATGATCATCGCAATATATTCACTGATCCCCATAGACTGCTGATTGC  
AGTATTATATGCTTGTGTTGATGAGGATGAGTGGCAATATCTTATATCCTCGAATTGTAGGAAGTGTTA  
TGAAAGGTCATCCAATCAGATTTTAGTTTACTTTTGTGTCAGCAATATCTATGGGTGATGTTGAATG  
ATTGTCAGTGGCAACCAATTCTATCTTGAAGAAAATTTCTAAGTCTTATCCCCTTTGTATGAAAATCA  
TAAATAATGAAGAAGCAAGAGAAAGAGAATTAGCTAAGCTCGAGCACCACCACCACCACCCTGA

Fig 97

## 2 CFE 81 "homologue of SEQ. ID NO. 77"

ATGTATCAAGGACTTTATCGAAAATATAGAAGTCAAAAGTCTCTCCAGTTAGTTGGTCAAGAAAGTTGTGG  
CTAAGACTCTTAAACAAGCGGTGGAGCAAGAGAAAATAAGTCACGCTTATCTTTTCTGGTCTGCTGG  
AAGCGGAAAAACAGTGTGCTAAAACTTTGCCAAGGCTATGAAGTGTCCCAATCAAGTGGGTGGCGA  
ACCTTGAATAACTGCTATATTGTCAAGCAGTGACGGACGGTAGTTTGAAGATGTCAATGAAATGGAT  
GCAGCTCTAATAATGGGGTAGATGAATTCGGCAAAATCGTGATAAATCTACCTATGCGCCTAGCCTTG  
CTCGTTAAAGGTTTATATCATAGATGAGGTTCCAGTCTGTCTACAGGGGCTTTAATGCCCTCTTAAAG  
ACCTGTGAAGAACCAACACAGAATGTAGTCTTATTTTGGCCACTACTGAATTGCAACAAGATTCCCTGTA  
CTATTCTATCCCCTGTGCAACGTTTGAAGTTTAAATCAATTAAGACACAGGATATTAAGGAACATATTAC  
TATATCTTAGAAAAAGAAAAATATCAAGTCTGAACAGAGGCTGTGGAAATCATTGCCAGACGGGCGGAA  
GGTGAATGCGGGACGCCCTTGCTATTTGGATCAAGCCCTGAGTTTGACACAGGGAAATGAGGTGACGA  
CTGCTATCTCTGAAGAAATTAAGTGGCACCATTAGCCTACAGCCTTGATGATTATGTGGCGGCTTGTCT  
CAACAGGATGTTCCCAAAAGCTTTGTCTTGCTTGAATCTTCTTTTGACAAATGGTAAGAGCATGACTCGTT  
TGTACCGATCTTTTGCACTATTTAAGAGACTTGTAAATTGTTCAAAACAGGGGGAGAAAATACTCATCAT  
AGTTCAGTCTTTGTAGAAAAATTTGGCACTTCTCAAAAAAATCTGTTTGAATGATTCGCTTAGCAACAGT  
GACTTTAGCAGATATTAAGTCTAGTTTGCAGCCCAAGATTATGCTGAAATGATGACCGTCCGTTTGGCG  
GAAATCAAGTCCGAACCAAGCTCTATCAGGAGCGGTTGAAAATGAAATGCTACGCTGAGACAGGAAGTT  
GCCGCTGTCAAAACAAGAGCTTTCTAATGTAGGTGCGGTTCTTAAACAAGTTGCACCAGCTCCTAGTCCAC  
CAGCTACGGGCAAAACAGTCTATCGTGTGATCGCAATAAAGTGCAATCTATCTTACAAGAGGCGCTGCA  
AAATCTGATTTAGCACGTCAAAATTTAATTCGTTTGAGAATGCCTGGGGAAGGTAATTGAAAATGCTA  
GGTGGGCGGAACAAGCTCTGCTCGAGCACCACCACCACCACCCTGA

Fig 98

## 2 CFE 82 "homologue of SEQ. ID NO. 78"

ATGTTTCAATTAAACCAATAAGTTAGCGGTATCGAACTTGATTAAAAACCGCAAACTGTACTATCGTTTGGC  
GCTGGCTGTTCTCTTGGCAGTCACTGTACCTATCTCTTTTACTCTCTAACCTTCAATCCTAAGATTGGGA  
AATCGTGGAGGAACAACCATTCAGGCTACACTTGGATTGGTATGTTTGTCTACCCCTTGCCTCAGCC  
ATTATCGTCTCTATGCCAATAGTTTGTGATGAAGAACCGTTCCAAGGAACTAGGAATTTATGGCATGTT  
GGCTTGGAGAAGCGTCACTTATCAGTATGACCTTTAAGGAGTTAGTGGTATTTGGGATTCTAACTGTTG  
GAGCGGCTATCGGTATTGGAGCCTTGTGTTGACAAGTTAATTTCCGCTTCTGCTCAAAGTAAATGAAATTG

Fig 99

2 CFE 82 (contd.)

Fig 99 (contd.)

AAGGTTGAGCTGGTTGCTACCTTCCAGACGAAAGTTGTCATTACAGTGCTTGTGTCTTCGGTTTGATTTT  
 CCTAAGGCTCAATGTTCTGAATGCCCTTCGAATCGCCCGTATGAATGCCCTCCAGCTCTCTCGTGAGAAAC  
 CTAGTGGAGAGAAAAAAGGTCGCTTCCTTCCTCCAAACCATTCTTGGTTCCTAAGTTTAGGAATTGG  
 CTATTATCTTGGCCTTACGGTAAAGATCCTCTTACAGCCTTAAACAACCTTCTTCATAGCTGTTTTACTGG  
 TATCTTGGGACTTATCTCTTGTAAATGCAGGGATTACCGTTTTCTCCAAATCTTAAAGAAAAATAAGA  
 AATACTATTACCAACCAAATAACCTCATATCTGTTTCTAACTTGATTTTCCGTATGAAGAAAAATQCAGTI  
 GGACTAGCCACCATCGCTATCTTGTCAACAATGGTTTTGGTAACCATGTCAGCAGCGACAAGCATTITCA  
 ATTCTTGAAGAGCTTTAAAAAAGTTCTAAATCCTCATGATTTTGGGGTTTCAGGGCAAAATGTTGAAAA  
 AGAAGACTTGGACAAACTCTTGAGCCAGTTTGCAAGTGACAAAGGTTATAAGATTAAAGAAAAAGAGT  
 ATTCTGTACACTTACTTTGCTGTGCGAATCAAGAAGGAACCAAGTTAACTATTTTGAAGAAAGGACAA  
 AACCGTGTCCAACCAAAAAACAGTTTTCATGGTATTTGACCAAAAAAGATTATGAAAAATGACTGGTCAAA  
 AACTGTCTCTATCAGGAAATGAGGTGCGACTCTTTGCAAGAATGAGGGAGTTAAAGAAACAGAAAGCTC  
 TAACTGTAAATGATCATCAATTTTCTGTAAAGAAAGAAATTTACTAAAGATTTTATGTCAACCATGTTCCA  
 AATCAGTTAATATTTTGAAGTGTGATTACAATTACCTTGTGTACCTGATTACAAGCCTTTTGGATCAA  
 TTCCAGATTGGGCTATCTATAATCAGTTTACGGTGGTATGAATGTAAATGCCAGTGAAGCAGAAACAAC  
 TCAAGGTCGCTGAGGAGTATGAAAAATACTTACAAAAGTTAATGCTCAATTAACACTGAAGGTAACTA  
 TGTGTAGGTAGCACTCTAGCAGATGCTAGTCTCAGATGAGTGCCCTCTTTGGTGGTGTCTCTTTATCG  
 GTATTTCTTATCCATTATCTTTATGGTGGAAACCGTCTGCTCATCTACTACAAACAAATTTCTGAAGGA  
 TATGAAGACCGTGAAGCGCTTTATATCTTGCAGAAAGTCGGTTTAGATCAAAAGCAAAATCAAGCAAAACA  
 TCAAAACACAGGTTTAACTGTATTCCTCTCTCTTGTCTTTGCTTCTCTACATCTAGCCTTTGGCTACC  
 ATATGCTTAGTCTGATTTTAAAGTGATTTGGTGTACTGGATACGACTATGATGTTGATTGTGACCTTGTCT  
 ATCTGCTCTATCTCTCATCGCTATGTGCTGATTTTCATGATTACTTCAAGAGTTATCGCAAGATTGT  
 GCAAAATGCTCGAGCACCACCAACCACCACCTGA

## 2 CFE83 "homologue of SEQ. ID NO. 79"

ATCAAAACAAGATCAACTAAAGGCTTGGCAACCAGCTCAGTTTGACCGTTTTGTCCGTATCTTAGAACAAG  
 ACCAGCTCAATCACGCCTATCTCTTTTCAGGTTCTTTGGAAGCTTGGAAATGGCGCAATTTTGTAGCTAAG  
 AGCCTTTTGTACGGATAAAGTTGGCGTCTTACCATGTGAGAAATGCCGAAGTTGCAAGCTGATGAAAC  
 AGGAAGAGTTTCCAGATGTCACTTGAATTAAGCCAGTCAATCAGGTCTATCAAGACAGAACGCATTTCGGG  
 AATTGGTGGGACAGTTTCTCAAGCAGGGATTGAAAGCCAGCAACAAGTCTTTATCATCGAGCAAGCGG  
 ATAAAAATGCATCCCAACGCAGCCAAATCTCTGCTCAAGGTCATCGAAAGAACCCAGAGTGAAGTTTATAT  
 TTCTTGTGACTAGCGATGAGGAAAAAGATTTACCGAATCCGAAGTCCGACTCAGATCTTCCACTTT  
 AAAAAGCAAGAAGAAAACTTATCTTACTCTTAGAACAATAAGGACTTGTAAAGAAAAAGCGACTCTT  
 TTAGCTAAGTTTAGTCAATCGCGAGCTGAAGCAGAAAAAGTTGGCACATCAGGCAAGTTTGTGACCTTGG  
 TCGATGAAGTGAACGCTGTGACTTGGTTAGTAGCTAAGAAAAAGAAAGTTATCTACAGGTTGCECA  
 AATTAGCAACTTGGCAGATGATAAGGAAAAACAGGATCAGGTTTACGGATTCTTGAAGTTCTCTGTGG  
 GCGGAGCTCTTGCAGGTAAGAGTAAGAGTAAATCTACAAGATTTACTAGAAGCTAGAAAAATGTGGCA  
 AGCTAAATGTCAGCTTTCAAAATGCCATGGAATATCTGGTCTTGAAGAAATACTCGAGCACCACCACCAC  
 CACCACCTGA

## 2 CFE84 "homologue of SEQ. ID NO. 80"

ATGAATTCAATTAATAAATTCTTAAAGAGTGGGGATTATTCCTCCTGATTCTGTCTATTACTAGCTTTGAG  
 CCGTATGTTTTTTGGAGCAATGTTTCGGTAGAAGGACATTCCATGGATCCGACCTAGCGGATGGTGAA  
 ATCTCTTTGTGTGTTAAGCACCTCCCTATGACCCTTTTGATATCGTGGTGGCCATGAGGAAGATGGCAA  
 TAAGGATATCGTCAAGCGCTGATTGGAATGCCGCGGACACCATTCGTTACGAAAAATGATAAACTCTAC  
 ATCAATGACAAAGAAACGGACGAGCCTTATCTAGCAGACTATATCAAACGCTTCAAGGATGACAAAGTC  
 CAAAGCACTTACTCAGGCAAGGGCTTTGAAGGAAATAAAGGAACCTTCTTTAGAAGTATCGCTCAAAAA  
 GCCCAAGCCTTACAGTTGATGTCAACTACAACCAACTTTAGCTTTACTGTTCCAGAAGGAGAATACC  
 TTCTCTCGGAGATGACCGCTTGGTTTCGAGCGACAGCCGCCAGTAGGTACCTTCAAAGCAAAAGATAT  
 CACAGGGCAAGCTAAATTCGGCTTCTGGCCAATACCCGTATCGGAACATTTCTCGAGCACCACCACCAC  
 CACCACCTGA

## 2 CFE85 "homologue of SEQ. ID NO. 81"

ATGGTAGTATTTACAGGTTCAACTGTTGAAGAAAGCAATCCAGAAAGGATTGAAAGAAATTAGATATTTCAA  
 GAATGAAGGCTCATATCAAAGTCAATTTAGGGAGAAAAAGGCTTTCTGTCTATTGTTAAAAAACC

2CFE85 (contd.)

Fig 102 (Contd.)

AGDCCAAGTGGATATTGAAGCGATTAGTGAACGACTGTTGTCAAAGCAAATCAACAGGTAGTAAAAGG  
CGTTCGAAAAAATCAATGATTTGAACGAGCGCTGTGAAGACGGTTAGTGAAGAAACCGTTGACCTTGCT  
CATGTGGTTGATGCTATTAAAAAATAGAGGAAGAAGGTCAAGGTATTTCTGATGAAGTCAAGGCTGAA  
ATCTTAAACATGAAAGACATGCCAGCACTATCTTAGAAGAAACTGGTCACATTGAGATTTTAAATGAAC  
TTCAAATCGAGGAAGCGATGAGGGAAGAAGCAGGCGCTGATGACCTTGAAAACCTGAGCAAGACCAAGCTG  
AAAGTCAAGAACTAGAAAGACTTGGGCTTGAAAAGTTGAAAACGAACTTTGATATTGAACAAGTAGCTACGG  
AAATAATGGCTTATGTTCAAACGATTATGATGACATGGATGTTGAGGCTACACTTTCAAATGATTATAA  
CCGTCTAGCATCAATCTACAAATTGACACCAACGAACCAAGGTCGTATTATCGGCTACCATGGTAAAGTC  
TTGAAGCCCTTGCAACTGTGGCTCAAAATTATCTTTACAACCGCTATTCAGAACCTTCTACGTTACAAT  
CAATGTCAATGATTATGTCGAACACCGTGCAGAACTCTGCAGACCTATGCGCAAAAATTGGCGACTCGT  
CTTTGCAAGAAGGGCGCAGTCATAAAACAGATCCAATGTCAAATAGCGAACGCAAGATTATCCATCGT  
ATTATTCACGTATGGATGGCGTACTAGTTACTCTGAAGGTGATGAGCCAAATCGCTATGTTGTTGTAG  
ATACAQAACCTGGAQCACCACCACCACCACCTGA

## 2CFE86: "homologue of SEQ. ID NO. 82"

Fig 103

ATGTCAATTTTCCATTATTTTAGCAGCGGGTAAAGGGACTCGCATGAAATCTGATTTGCCAAAAGTTT  
GCACAAGGTTGCGGGTATTTCTATGTTGGAACATGTTTTCCGTAGTGTGGGAGCTATCCAACCTGAAAAAG  
ACAGTAACAGTTGTAGGACACAAGGCAGAAATTGGTTGAGGAGGTCTTGGCTGAACAGACAGAAATTTGTG  
ACTCAATCTGACAGTTGGGAAGTGGTCATGCACTATGATGACAGAGCCTATCTTAGAAGGTTTGTGTCAG  
GACACACCTTGGTCACTTGCAGGAGATACCTCTTTAATCACTGGTGAAGCTTGAAAAACTTGATTGATTT  
CCATATCAATGATAAAAAATGTGGCCACTATCTGACTGCTGAAACGGATAATCCTTTTGGCTATGGACGA  
ATTGTTGTAAATGACAATGCTGAGGTTCTTCGTATTGTTGAGCAGAAAGGATGCTACAGATTTTGAAGAAGC  
AAATCAAGGAATCAACACTGGAACATACGCTCTTTGACAACGAGCGTTTGTGTTGAGGCTTTGAAAAATAT  
CAATACCAATAACGCTCAAGGCGAATACTATATTACAGACGTCATTGGTATTTTCCGTGAAACTGGTGAA  
AAAGTTGGCGTTTACTTTGAAAAGATTTTGATGAAAGTCTTGGGGTAAATGACCGTGTGGCGCTTGCGA  
CAGCTGAGTCAGTTATGCGTCTGCGCATCAATCAATAACACATGGTCAACGGTGTAGCTTTGTCAATCC  
AGAAGCACTTATATCGATATTGATGTTGAGATTGCTCCGGAAGTTCAAATCGAAGCCAATGTTATCTTG  
AAAGGGCAAAACGAAAATTGGTGCTGAAGACTGTTTGACAAACGGTACTTATGTAGTGGACAGCACTATC  
GGAGCAGGAGCGGTCAATACCAATTCATGATTGAGGAAAGTAGTGTGCAAGCGGTGTGACAGTCCGT  
CCTATGCTCACATTCGTCCAAATTCAGTCTGGGTGCCCAAGTTCATATTGGTAACTTTGTTGAGGTGAA  
AGGATCTCAATCCGTGAGAAATACCAAGGCTGGTCAATTTGACTTATATCGGAAACTGTGAAGTGGGAAGC  
AAGCTTAAATTTGGTGCTGGAACATTAACAGTCAACTATGACGGCAAAACAAATACAAGACAGTCATTG  
GAGACAATGCTTTGTTGGTTCAAATTCACCATTAATTGACCAAGTAGAACTTTGGTGACAATTCCTCTCT  
GCTGCTGTTGAACTATTACTAAAGACGTGCCAGCAATGCTATTGCTATTGGTCCGGTCCGTCAATCA  
ATAAAGCAATATGCAACACGCTCTCTCATCATCTTAAGAACCAAGCTCGAGCACCACCACCACCACCA  
CTGA

## 2CFE87: "homologue of SEQ. ID NO. 83"

Fig 104

ATGTCCAAGATTCTAGTATTTGGTCAACAAAATCCAGACTCAGATGCCATCGGGTCACTCTGTAGCTTTTGC  
CTACCTTCCAAAAGAGCTTACGGTTTGGATACGGAAGCTGTTGCCCTTGGAACTCCAAATGAAGAAACA  
GCTTTGCTTGAACATTTTGGTGTGGAAGCACCAGCTGTTATCACTTCTGCCAAAGCAGAGGGGCGAG  
AGCAAGTTATCTTGACTGACCACAATGAATTCCAAACATCTGTATCAGATATCCGTGAAGTAGAAGTTTA  
CCTGTTGTAGACCAACCAAGGTGTGGCTAACTTTGAAACTGCAAGCCCACTTTACATGCGTTTGGAGCCA  
GTTGGATCAGCGTCTTCAATCGTTTACCGTATGTTCAAAGAACATGGTGTAGCTGTGCCTAAAGAGATTG  
CAGGTTTATGCTTTACAGGTTTGAATTCAGATACCTTCTTTTGAATCAACCAACAACACACCCAACAGAT  
AAAATCATTTGCTCTGAAATTGGCTGAATTGGCTGGTGTAAACTTGGAAGAAATATGGTTTGGCAATGTTGA  
AAGCTGTACCAACTTGGCTAGCAAAATCTGCTGAAGAAATGATTGACATCGATGCTAAGACTTTTGAAC  
CAACGGAAATAATGTCGTGTTGCCCAAGTGAACACAGTTGACATCGCTGAAAGTTTTGGAACGCCAAGCA  
GAAATTTGAAGCTGCAATGCAAGCTGCCAAGCAATCAAACGGCTACTCTGACTTTGTCTTGATGATTACAG  
ATATCOTCAACTCAAACCTCAGAAATATTGGCTCTTGGTGCCAATATGGACAAGGTGGAAGCGGCTTTCAA  
TTTCAAACCTTGAAAACAAATCATGCTTCTTGTGCTGGTGGCGTTTACGTAAGAAACAAAGTGGTACCTCAAT  
TAACCTGAAAGCTTAAATACGCTCGAGCACCACCACCACCACCTGA

Fig 105

## 2CFE88: "homologue of SEQ. ID NO. 84"

ATGATTTCAAAGAGATTAGAATTTGGTAGCTTCTTTGTGTACAGGGGGCTATTTTACTAGATGTGGGAA  
GTGACCAATGCTTATCTGCCTATCGAGTTGGTTGAGAGAGGGCCAAATCAAAGCGCTATTGACAGGTGAGGT



2CFE 88 (contd)

Fig 105 (contd)

GGTGGAGGTCCCTATCAGTCTGCGGTTAAAAATGTTGAGGCTCACGGCCTAAAGGAGAAAATCCAAGT  
 CCGTTTAGCCAATGGCTTGGCAGCTTTTGAAGAGACTGACCAAGTGTCTGTCAATTACCATTGGCTGGCATG  
 GGTGGTGGTTGATTGCTAGGATTTTGAAGAAGGTTTGGGGAAGTTAGCTAATGTAGAGCGTTTGTATCC  
 TCGAGCCCAATAATCGTGAAGACGACTTGCCTATCTGGCTACAGGATCATGGATTCCAGATTGTAGCAGA  
 AAGAATCTTAGAAGAAGCTGGAAGTTTTATGAGATTTTGGTGGTGOAAGCAGGACAAATGAAAGCTATC  
 AGCCAGTGATGTTCCGCTTGGTCCCTTCTTGTCAAAAGAGTCAGTCCAGTATTTGTCCAAAATGGCAA  
 AAAGAAGCTGAGAAGCTAGAATTCCGCCCTCGGACAAATCCCAAAAAAATCTGGAAGAAGCTCAAGTT  
 CTAGTAGATAAGATTCAAGCTATCAAGGAGGTGCTCCATGTTAGCAAGCTCGAGCACCACCACCACCACC  
 ACTGA

Fig 106

2 CFE89 "homologue of SEQ. ID NO. 85"

ATGAATTAAACGATATTAAGACTTGATGACTCAATTTGACCAGTCAAGTTTGAGAGAATTTTCTTATA  
 AAAATGGGACGGATGAGTTGCAGTTTAGCAAGAATGAAGCAAGACCTGTGCTGAAGTTGCAACTCAAG  
 TCGCTCCAGCACCGTTCTAGCAACACCGAGTCCAGTAGCTCTACATCTGCTCCAGCAGAGACTGTAGC  
 AGAAGAAGTTCCAGCTCCAGCTGAAGCAAGTGTGGCTACTGAGGGAAATCTTGTAGAGAGTCCACTTGT  
 GGAGTGGTTTACTTGGCTGCTGGACCAGATAAACCTGCCTTCTTACAGTTGGTGATAGTGTCAAAAAAG  
 GTCAAAACATTGTAATTATCGAAGCCATGAAAGTCATGAATGAAATCCAGCTCTAAGGATGGTGTGGT  
 AACGGAATTTCTCTCTTAACGAAGAAATGGTTGAGTTTGGTAAAGGATTGGTACGTATCAAACTCGAG  
 AACCAACCACCACCACCTGA

Fig 107

2 CFE90 "homologue of SEQ. ID NO. 86"

ATCAAACTAAATCGAGTAGTGTAACAGGTTATGCAAGTAACATCTCCAATCGGAAATACACCAGAAGAA  
 TTTTGGAAATAGTTTAGCAACTGGGAAATCGGCATTGGTGGCATTACAAAATTTGATCATAGTGACTTTG  
 ATGTGCATAATGCGGCAGAAATCCAAGATTTTCCGTTTCGATAAATACTTTGTAAGAAAGATACCAACCG  
 TTTTGAATACTATTCTTATATGCTTGTATGCAGCCCAAGAGGCTGTAAACCATGCCAATCTTGTATGTAG  
 ACGCTCTTAATAGGGATCGTTTTGGTGTATCGTTGCATCTGATTTGGTGGAAATCAAGGAAATGAAGA  
 TCAGGTACTTGGCTTCATGAAAAAGGACCCAAACGTTGCAAAACCAATGACTCTTCCAAAAGCTTTACCA  
 AATATGCTTCTTGGAAATGTAAGCATGCGTTTTGGTGCAAAACGGTGTGTGTAATCTATCAATACTGCCGT  
 CTGTCATCAAAATGATGCGATTGGGGATGCTTCCGCTCCATTAAGTTTGGFTTCCAAGATGTGATGTTGG  
 TGGGAGGAACAGAAGCTTCTATCACACCTTTTGGCATCGCTGGTTTCCAAGCCTTAACAGCTCTCTACT  
 ACAGAGGATCCAACTCGTGCTTCGATCCCATTTGATAAAGGATCGCAATGGGTTTGGTTATGGGTGAAGGTT  
 CAGGGATGTTGTTGTAGAAAGTCTTGAACACGCTGAAAAACGTTGGAGCTACTATCTGGCTGAAAGTGT  
 TGGTTAGGAAATACCTTGTGATGCTTACCACATGACTTCTCCACATCCAGAAGGTCAGGGAGCTATCAAG  
 GCCATCAAACTAGCCTTGGAAAGAAGCTGAGATTTCTCCAGAGCAAGTAGCCTATGTTAATGCTCAGGAA  
 CGTCAACTCCTCCCAATGAAAAAGGAGAAAGTGGTGCTATCGTAGCTGTTCTTGGTAAGGAAGTACCTGT  
 ATCATCAACCAAGCTTTTACAGGACATTTGCTGGGGCTGCGGGTGCAGTAGAAGCTATCGTACCATC  
 GAAGCTATGCGTCAATACTTTGTACCAATGACAGCTGGGACAAAGTGAAGTATCAGATTATATCGAAGCTA  
 ATGTCGTTTATGGACAAGGTTTGGAGAAAGAAATCCATACGCTATTTCAAATACTTTTGGTTTGGAGGC  
 CAGAAATGCAAGTTCTTGCTTCAAACGTTGGGAGAAATAGACTCGAGCACCACCACCACCACCCTGA

Fig 108

2 CFE91 "homologue of SEQ. ID NO. 87"

ATGAACATCTATGATCAACTACAAGCTGTAGAAGACCGTTATGAAGAACTAGGAGAAATGCTGAGTGAC  
 CCTATGCTGTTTCAGACACCAAGCGTTTTATGAGCTTTCAAAGAAAGAGCTTCCAATCOTGACACCG  
 TAATAGCTACCGTGAGTATAAACAAGTCTTCAAATATCGTCGATGCGAAGAGATGATTAAGGAATC  
 AGCCGAGATGCGGACTTGGAAAGAAATGGCCAAGCAAGAACTCAAAGATGCCAAGGCTGAAAAAGAAAG  
 AATATGAAGAAAACTGAAAAATTTGCTCCTTCCAAGGATCCAAACGATGCAAGAAATATCATCTTGA  
 AATCCGTGGAGCAAGCTGGTGGAGACGAAGCGGCACTTTTCGCTGGAGATTGCTAACTATGTACCAAAAG  
 TATCGGGAAGCCCAAGGTTGGCGCTTTGAAGTCATGGAAGCCTCTATGAATGGTGTGGTGGTTTAAAG  
 AAGTGGTTGCTATGGTTTCAAGTCACTGTATACTCTAAGCTTAAGTATGAATCAGGTGCCCCACCGTGTG  
 CAACGTGTTCCGTGTACAGAAAGCCAAAGGCGGTGTCATCTTCCAGAGCGACAGTCTTGTATATGCCAG  
 AAGTTGAAGAGGTTGAATACGACATTGATCCAAAAGACCTTCGTGTGACATCTATACGCGCTCTGGTGC  
 TGGTGGACAGAACGTCAATAAGGTTGCGACTGCGGTTCTGATCGTTCACTTGCCAACCAATATCAAGGTT  
 GAGATGCAAGGAAGAACGTACCCAGCAGAAAGAACCGGAGAAAGGCTATGAAGATTATCCGTGCACGCGTC  
 GETGACCACTTTGCTCAGATTGCTCAGGATGAACAAGACGCTGAGCGTAAGTCAAGTCAATCGGTACTGGTG  
 ACEGTTCAAGAGGATCCGAACCTTAACTTCCCAAAAACCGTGTCAAGACCACCGTATCGGCTTGAC



(contd)

Fig 108

2 CFE 91 (contd)

CCCTCCAAAACTAGATACGATTTTGTCTGGTAAATTGGACGAAGTTGTGGATGCCTTGGTGCTTTATGACC  
 AAACACAAAACTAGAAGAATTAAACAACTCGAGCACCACCACCACCACCACTGA

2 CFE 92 "homologue of SEQ. ID NO. 88"

ATGGCTACACTCTTAAACCTGAAGAAATCGGCGTTTGGCCATCGGTGGTCTAGGAGAAATCGGGAAAA  
 AACTTACGGAATTGAATACCAAGACGAGATTATCATCGTCCGATGCTGGGATTAAATCCCAGAAATGA  
 CTTCCTTGGTATCGACTATGTATTCTGACTACTCTTACATCGTAGACAATATCGACCGGTCAAGGCTG  
 TTATAACACACACGGACACGAGGACCACATTGGTGGGATTCGGTCTCAAGCAAGCAAAATGTCCC  
 TATTTATGCTGGACCGCTTGCCTTGGCTTTGATCCGTGGGAAACTCGAAGAACACGGCCCTCTTGGCAAC  
 QCCAACTTTACGAAATCAACCACAACCCGAGTTGACCTTTAAAAATCTCAAGGCAACTTTCTTAGAA  
 CGACTCACTCTATTCCAGAGCCTTTGGGGATTGTCATTTCATACTCTCAAGGGAAAAATCGTCTGTACGGGT  
 GACTTTAAGTTCGACTTTACTCCAGTTGGAGAACCTGCGGACTTGCAATCGTATGGCTGCGCTTGGTGAAG  
 AAGGCGTGTCTGTCTCTGTCTGACTCGACAAATCGGGAAGTACCAACCTTTACCAACTCTGAAAAAGT  
 CGTGGCTCAGTCATTATGAAGATTATCCAAGGTATTGAAGGACGTATCATCTTTGCATCTTTGGCTCAA  
 ATATCTTCCGTCTCCAGCAGGCAACAGAAAGTGTGTTAAGACTGGACGCAAGATTGCGGTCTTTGGTCC  
 TTTCTATGAAAAGGCCATTGTCAACGGAATCGATCTTGGCTACATCAAAGCTCCTAAGGGAACTTTATC  
 QAGCCAAATGAAATCAAAGATTATCCTGCAGGAGAAAGTTCTTATCTCTGTACAGGTAGTCAGGGTGAGC  
 CTATGCGAGCCCTCTCTCGTATCGCCAACGGAACCCACCGTCAAGTACAATTACAACCAAGGTGATACCGT  
 TATCTTCTCTTCTAGTCCCATCCCTGGAAACACTACTAGCGTCAACAAGCTGATTAAACATCACTTTCTGAAG  
 CTGGTTCGAAAGTTATCCACGGTAAAGTGAACAAATATCCATACATCTGGACACGGTGCCAGCAAGAGC  
 AAAAACTCATGCTCCGCTTGAATTAAGCCAAAACTTCTCATGCTGTCCACGGTGAATACCGCATGCAAAA  
 AGTCCACGGTGGACTAGCAATGGATACTGGTGTGTGAAGGACAATATCTTTATCATGAGCAATGGCGAT  
 GTCTTCCCTTACTGCTGACTCAGCTCGTATCGCAGGTCAATTTCAACGCCCAAGATATCTATGTCGATGG  
 AAATCGTATCGGTGAAAATGGCGCAGCTGTCTCAAAGATCGTCCGATCTATCTGAAGACGGTGTCTGT  
 CTAGCAGTCCCAACTGTTGACTTCAAATCGCAGATGATTCTGTCTGGGCCAGATATCTCTCAGCCGAGGCT  
 TTGTCTACATGAGAGAGTCTGGAGACTTGATTCCGCCAAAGCCAGCGTATCTCTTCAATGCCATTCTGATC  
 GCACTGAAAAATAAGGATGCTAGCGTGCAATCTGTCAA  
 TCTATGAAAAATACCGAACGTGAACCGATCATCATCCCG/  
 CCACCAACCAACCACTGA

Fig 109

2 CFE 94

ATGGCTACGGCAACAAAAAGAAAAATCAACAGTTA/  
 AAGGCCAAGACGATTGAAAAATATCTAGGCAGAACTACAAGGTTTAGCCAGTGTGCGGCATATCCGT  
 GATTTGAAGAAATCCAGTATGTCCGTGATTTGAAAAATAATTATGAACCGCAATATATTAATATCCGAG  
 GAAAGGCCCTCTTATCAATGACTTGAAAAAAGAAGCTAAAAAAGCTAATAAAGTTTTCTCGCGAGT  
 ACCCGACCGTGAAGGAGAAGCGATTCTTGGCATTGGGCCATATTCTCAACTTGGATGAAAATGATGC  
 CAACCGTGTGGTCTTCAATGAAATCAACCAAGGATGCAAGTCAAAAAATGCTTTTAAAGAACCTCGTAAGATC  
 GATATGCACTTGGTGGATGCCCAACAAGCTCGTCCGATCTTGGATCGCTTGGTAGGGTATTGATTTCCG  
 CTATTTTGTGGAGAAGGTCAAGAAGGGCTTGTACGAGGTGCGGTTCAGTCCATTGCCCTTAAACTCAT  
 CATTGACCGTGAAAAATGAAATCAATGCCTTCCAGCCAGAAAGAACTGAGACAGTTGATGCTGTCTTTAAA  
 AAGGGAACCAACAATTTATGCTTCTCTATGGAGTAOATGGTAAAAAGATGAAACTGACCAGCAAT  
 AAGGAAGTCAAGGAAGTCTTGTCTCGTGTGACGAGTAAAGACTTTTCAATAGATCAGGTGGATAAGAAA  
 GAGCGTAAGCGCAATGCTCCTTTACCTATACCACTTCACTATGCAAGATGGATGCTGCCAATAAAATCA  
 ATTCCGTACTCGAAAAACCATGATGGTTGCCCAACAGCTCTATGAAGGAATTAATATCGGTCTGGTGT  
 TCAAGGTTTGATTACCTATATGCGTACCGATTTCGACTCGTATCAGTCCGTGTAGCGCAAAATGAGGCGGCA  
 AGCTTCAATTACGATCGTTTTGGTAGCAAGTATTCTAAGCAAGGTAGCAAGGTCAAAAAACGCATCAGGTG  
 CTCAGGATGCCCATGAGGCTATTCTGTCGCTCAAGTGTCTTTAATACACCAGAAAGCATCGCTAAGTATCT  
 GGACAAGGATCAGCTCAAGCTATATACCGTTATCTGGAATCGTTTTGTGGCTAGCCAGATGACAGCGGCC  
 GTTTTGTATACGATGGCTGTTAAATTTGTCTCAAAAAAGGGGTCAATTTGCTGCCAATGGTAGTCAGGTAA  
 GTTTGATGGTATCTTGCCATTTATAATGATTCTGACAAGAATAAGATGTTACCGGACATGGTTGTTGGAG  
 ATGTGGTCAAAACAGGTCAATACCAAAACAGAGCAACATTTCAACCAACCGCTGCCCGTTATTCTGAAGC  
 AACACTATTAAACCTTAGAGGAAAAATGGGTGGAGCTCCATCAACCTACGCGCCAACCATTTGAAC  
 CATTCAGAAAGTTATTATGTTCCGCTGGCAGCCAAACGTTTTGAACCGACAGATGTTGGAGAAAAATGTC  
 AATAAGCTCATGTTGAATATTTCCAGATATCGTAAACGTGACCTTCAAGCTGAAATGGAAGTTAAAC  
 TGGATGATGCGAAGTCGAAAAAGAGCAGTGGCGACGGGTCAATGATGCTTTTACAAACCATTTCTCAA

Fig 110

JCFE 94 (contd)

Fig 110 (contd)

ACGAAGTGGCAAGGCTGAAGAAGAAATGGA AAAAATCCAGATTAAGGATGAACCAGCTGGATTTOACTG  
 TGAAGTGTGTGGTAGTCCAATGGTCATTAAACTTGGTCGTTTTGGTAAATTTCTACGCTGTAGCAATTTCC  
 CAGATTGCCATCATACCCAAGCAATCGTGAAAGAGATTGGTGTGAGTGTCCAAGCTGTCTACAGGGACA  
 AATTATTGAGCGAAAAACCAAGCGTAATCGCCTATTCTATGGTTGCAATCGCTATCCAGAATGTGAATTT  
 ACCTCTTGGGACAAGCCTGTTGGTGGTGAAGTGTCCAAAATGTGGCAACTTCCACATGGAGAAAAAAGTCC  
 GTGGTGGTGGCAAGCAGGTTGTTGTAGCAAAGGCGACTACGAGGAAGAAAAAGATGGCTCTTTGTCAACT  
 GCTCGAGCACCACCACCACCACCTGA

## 2 CFE95 "homologue of SEQ. ID NO. 91"

Fig 111

ATGTTTATTTCATCAGTGCTGGAATTGTGACATTTTACTAACTTTAGTAGGAATTCCGGCCTTTATCCA  
 ATTTTATAGAAAGGCGCAAATTACAGGCCAGCAGATGCATGAGGATGTCAAACAGCATCAGGCAAAAAGC  
 TGGGACTCCTACAATGGGAGGTTTGGTTTTCTTGATTACTTCTGTTTTGGTTGCTTTCTTTTCGCCCTATT  
 AGTAGCCAATTACAGCAATAATGTGGGAATGATTTGTTCATCTTGGTCTTGATGGCTTGGTCCGATTTT  
 AGATGACTTTCTCAAGGCTTTTCTGTAATAATCAATGAGGGGCTTAATCCTAAGCAAAAATTAGCTCTCAAG  
 CTCTAGGTGGAGTTATCTTCTATCTTTCTATGAGCGGGTGGCGATATCTGTCTGTCTTTGTTATCCA  
 GTTCATTTGGGATTTTCTATATTTCTTCTGCTCTTTCTGGCTAGTCCGTTTTTCAAACGCAGTAAACTTG  
 ACAGACGGTGTGACGGTTTAGCTAGTATTTCCGTTGTGATTAGTTTGTGCTATGGAGTTATTGCCCTA  
 TGTGCAAGGTCAGATGGATATTCTTCTAGTGATTCTTGCCATGATTGGTGGTTTGTCTGGTTCTTCATCTT  
 TAACCATAGCCTGCCAAGGCTTTATGGGTGATGTGGGAAAGTTTGGCCCTAGGTGGGATGCTGGCAGCT  
 ATCTCTATGGCTCTCCACCAGGAATGGAATCTCTTGATTATCGGAATTGTGATATGTTTGAACCAACTC  
 TGTATGATGCAAGTCAATTTTCAAAGTGACAGGTGTGTAACAGTATTTTCCGTATGACGCGCTGTACATC  
 ACCATTTGAGCTTGGGGGATTTGTCTGGTAAAGGAAATCCTTGGAGCGAGTGGAAAGGTTGACTTCTTCTT  
 TTGGGGAGTTGGTCTTCTAGCAAGTCTCCTGACCCTAGCAATTTTATATTTGATGCTCGAGCACCACCACC  
 ACCACCCTGA

## 2 CFE96 "homologue of SEQ. ID NO. 92"

Fig 112

ATGGCAGCGCAATTTTCACTTGAAAAAACTCGTAATATCGGTATCATGGCTCACGTCGATGCCGGTAAAA  
 CAACAACTACTGAGCGTATTCTTTACTACACTGGTAAAAATCCACAAAATCGGTGAAAACCTCACGAAGGTGC  
 GTCACAAATGGAAGTGGATGGAGCAAGAGCAAGAAGCTGGTATCACGATCACATCTGCTGGCAACACAGC  
 TCAATGGAACAACCAACCGCGTAAACATCATCCACACACCAGGACACGTGGACTTCACAAATCGAAGTACA  
 ACCTCTCTTGGTGTATTGGATGGTGGGTTACCGTTCTTGACTCACAATCAGGTGTTGAGCCTCAAACCTG  
 AAACCTTTGGCGTCAAGCAACTGAGTACGGAGTTCCACGTATCGTATTTGCCAACAAAATGGACAAAAT  
 CGGTGGTGAAGTCTTCTTACTCTGTAAAGCACACTTCACGATCGTCTTCAAGCAAAATGCACACCCAATCCAAT  
 TGCCAACTCGGTCTGAAAGATGACTTCCGTGGTATCAATTGACTTGATCAAGATGAAAGCTGAAATCTATAC  
 TAACGAACCTTGGTACGGATATCCTTGAAGAAGACATCCCAAGCTGAATACCTTGACCAAGCTCAAGAATAC  
 CGTGAAAAATTGATTGAAGCAGTTGCTGAAAGTACGGAAGAAATTGATGATGAAATACCTCGAAGGTGAA  
 GAATCTACTAACGAAGAAATTGAAGCTGGTATCCGTAAGCGACTATCAACGTTGAATTCTTCCGAGTAT  
 TGTGTGTTTCAAGCCTTCAAAAAACAAAGGTGTTCAATTGATGCTTGATGCGGTTATCGACTACCTTCCAAGT  
 CCACTTGACATCCCAACCAATCAAAAGGTATTAACCCAGATACAGACGCTGAAGAAAATTCGTCCAGCATCTG  
 ACCAAGAGCCATTGTCAGCTCTTGCCTTCAAGATCATGACTGACCCATTCTGAGGTCTGTTGACATTCTTC  
 CGTGTTTACTCAGGTGTTTCTCAATCAGGTTTACATCGTATTGAATACCTTCAAAGGTAAACGTGAACGTAT  
 CGACGTTATCCTTCAAAATGCAAGCTAACAGCCGTCAAGAAAATCGACACTGTTTACTCAGGTGATATCGCT  
 GCTGCCCTTGGTTTGAAGATACTACAACCTGGTGAATGACAGATGAAAAAGCTAAAAATCATCCTTG  
 AGTCAATCAAGTTCCAGAAACCAAGTTATCCAATTGATGGTTGAGCCAAAATCTAAAGCTGACCAAGACAA  
 GATGGGTATCGCCCTTCAAAAAATGGCTGAAGAAGATCCAACATTCGCGCTTGAACAAACGTTGAAACT  
 GGTGAAACAGTTATCTCAGGTATGGGTGAAGTTACCTTGACGCTCTTGTGATCGTATGCGTGGTGAAGT  
 CAAAGTTGAAGCGAAGCTAGGTGCTCTCAAGTATCTTACCGTGAAAACATTCGCGCTCTTACTCAAGCA  
 CGGGAATCTTCAAACGTCACTCTGGTGAAGGTCAATTGGGTGATGTATGGATTGAATTTACTCCAA  
 ACGAAGAAGGTAAAGGATTCCGAATTCGAAAACGCAATCGTCCGGTGGTGGTTCTCGTGAATTTATCCC  
 AGCGGTTGAAAAGGTTTGGTGAATCTATGGCTAACGGTGTCTTGCAGGTTACCAATGGTTGACGTT  
 AAAAGCTAAGCTTTATGATGGTTTATATCACGATGTGACTCATCTGAAACTGCCCTTCAAGATTGCGGCTTC  
 ACTTCCCTTAAAGAAGCTGCTAAATCAGCACAACCAAGCTATCCTTGAACCAATGATGCTTGTAAACAATC  
 ACTGTTCCAGAAAGAAAACCTTGGTGAATGTTATGGGTCAAGTAACTGCTCGTGGACGTGTAGATGGTA  
 TGGAAAGCACCGGTAACAGCCAAATCGTTCTGCTTACCTTCCACTTGGTGAATGTTTCCGTTACCGAAC  
 AGTTCTTCTGCTTGCATCTCAAGGACGTGGTACATTCATGATGGTATTTGACCACTACGAAGATGTACCTA

(cont'd)  
Fig 112

2 CFE 96 (cont'd)

AGTCAGTACAAGAGAAATTATTAAGAAAAATAAAGGTGAAGACCTCGAGCACCACCACCACCACCTG

2 CFE 97 "homologue of SEQ. ID NO. 93"

ATGCCAAATTACAATATTCATTTACCCGCTGATATCACAGAAGCAGAAATTGCTGAAGTAGCGGATA  
 CCTGCTTCTGTTGGATCACAACAGGTCTAAAACAAAAGAACTGGAGCGCCGCTTGCTCTTTACAC  
 ACAGACACCTAAGACTGTTTGTCTCAACTCTGCGACAGCCGCTCTGGAGTTGATTTACGCGTTTGGAAO  
 TGGAGCTGGTGATGAAGTCATCGTTCCAGCCATGACCTATACGGCTTCATGTAOTGTCATTACGCACGT  
 GGGAGCAACCCCTGTCATGGTGGATATCCAAGCAGATACGTTTGAATGGACTATGACCTGCTTGAGCAA  
 CCTATCACTGAQAAAACTAAGGTGATTATCCAGTAGAGCTCGCAGGGATTGTTTGGCATTATGACCGTT  
 TGTTCAGTGGTGGAGAAAAACGTGACTTCTTTACCGCTTCAAGCAAGTGGCAAAAGGCCCTTAAACCG  
 TATTTGCTATTGCTCTGATAGTGGCCACGCTTGGGATCTACTTATAAAGGAGAACCTTCTGGTTCTATCG  
 CTGATTACTTCTCTCATTCATGCTGTTAAGAACCTTACAACGGCAGAAAGTGGAAAGTGGCAGTTGG  
 AAAGCCAATCCAGTGAATGATGACGAAGAGATGTACAAGGAATTCAAAATCCTTTCCCTTCACGGGCAAA  
 CTAAGGATGCTCTTGCCAAAGATGCAACTGGGGTCATGGGAATACQATATCGTTACACCAGCCTATAAGTO  
 CACATGACCGATATCATGGCTTCACTTGGTTTGGTACAATTGGACCGCTATCCAAGTTTGTGCAACGGC  
 GCAAGGACATTGTGGACCGCTATGATAGTGGTTTGGCAGGTTCTCGCATCCATCCTTTGGCACACAAGAC  
 TGAACCTGTGCAATCTTCACGCCACCTCTACATCACCCGTGTAGAAGGAAGTAAGCCTAGAAGAACGCAAC  
 CTATCATCCAAGAAATTGGCTAAAGCAGGAATTGCAAGTAATGTTCACTACAAACCGCTTCTCTCTGA  
 CAGCCTATAAGAATCTTGGATTGATATGACGAACCTATCCTAAGGCCTATGCCTTCTTTGAGAATGAATT  
 ACCTCTCTCTTCACTAAATTAAGCGATGAAGAAAGTAAGCTATATCATTGAGACTTTCAAAACAGTTT  
 CTGAAAAAGTCTAATCTTATCAAAAAAATCGAGCACCACCACCACCACCTG

Fig 113

2 CFE 99 "homologue of SEQ. ID NO. 95"

ATGTTTATACTTATTGCGTGAATTAGTTGATTGCTCTTATGGTCCATCAATGGCAATGCTCACTATCAT  
 AATACTGATAAAATTCCTAATCAAGATGAAAATTATATTTAGTTGCGCTCACCGTACCTGGTGGGATC  
 CTGTTTATATGGCCTTTGGCAACCAAGCCAAAACAGTTTATCTTTATGGCAAAAAAGAACTCTTTACCAA  
 CCGTATCTTTGGTTGGTGGATTCGTATGTGTGGCGCCTTTCCCATCOACCGTGAATAATCCACGCGCTCAG  
 CCAACAATATCTATCAACGTTCTCAAAAAAAGTGACCGCTCTCTCATCATGTTTCCAAAGTGGTACCGC  
 CACTCAACGATGTCAAGGGGGCGCGCAGCACTGATTGGCAAAATGGCCAAGTCCGTATCATGCGGTT  
 ACCTCAACCGGTCCCATGACTTTGAAGGGCTTGATTAGCGGTGAACGTGTGATATGAACCTTTGGAAATC  
 CAATCGATATCTCAGATATCAAGAAAATGAATGATGAAGGCATTGAACAGTCGCAATCGTATTCAAA  
 CAGAAATCCAACGCTGAGCAGAAAGAAACGAAACAATGGCACAATGATAAAAAACCAATCCACTCTGGT  
 GCTTATCCGCTATCCCTGCCCTCATCTTGTATTATCCTCGCTATCCTAACCATCATCTTTAGCTTTATCG  
 CAAGCTTCATCTGGAACCCAGATAAGAAAAAGAAAGAACTTGCACTCGAGCACCACCACCACCACCT  
 GA

Fig 114

2 CFE 101 "homologue of SEQ. ID NO. 97"

ATGACCACGAATTTTACATTTTGAAAAAATCAGCCGCCAGACTTGGCAATCTTTACATCGAAAGACAA  
 CACCTCCTTTGACAGAAAGAAATTTGAATCTATCAAGAGTTTAAATGACCAAAATCAGTCTCCAAGACGT  
 TACAGATATCTATCTCCCTTGGCTCATCTGATTGAGATTACAAGCGAACTAAGGAAGATTAGCCTTTT  
 CAAAGGAATTTCTCCAAACGTGAAAGTAAATCTCAACCTTTTATTATTGGGGTTTCTGGGAGTGTGGC  
 GTTGGAAATTCACAACAGTGGCTACTTCAAAATCCTACTGTCCCGTACGTTTACAGATGCTACGGTTG  
 AGTTGTTACAACCTGATGGTTTCTCTATCCCAATCAAACCTTGATTGAGCAGGGGATTTAAATCGTAAA  
 GGATTTCTGAAAGCTATGATATGGAAGCTCTTCTCAACTCTTGGACCGCATCAAAAATGGACAAGATG  
 TAGATATCTCTGTCTATTCTCATGAAGTTTACGACATCGTACCCGAAGAGAAACAAAGTGTCAAAGCTGC  
 TGATTTGTAATTTGTTGAGGGAATCAATGTCTTCAAAAATCCACAAAACGATCGTGTCTATATCACTGACT  
 TCTTTGACTTTTCCATCTATGTAGATGGTGGAGTGGATGATATTGAAAAGTTGGTATCTGGACCGTTTCTT  
 AAAATGCTGAGTCTAGCCCAAAACGACCCTGATAGCTACTATTATCGTTTACTCAGATGCCGATTGGG  
 AAGTGGAAAGCCTTTGGCCATCAGGTCTGGACCAATATCAATCTCAGAAATCTACAAAATTATATTGAACC  
 AACCAATAATCGTGCAGAAATGATTCTTCATAAAAGCAAGAACCATGAAATCGATGAAATTTACTTAAA  
 AAAGCTGAGAACCAACCACCACCACCTGA

Fig 115

2 CFE 102 "homologue of SEQ. ID NO. 98"

ATGGAAATTTCAATTATTAACAGATGTTGGTCAGAAACGAAACAAATAACCAAGACTATGTCAACCACTATG  
 TCAATAGAGCTGGACGTACCATGATTATTTAGCTGATGGGATGGGAGGTCTATCGCGCAGGGAATATCGC

Fig 116

2 CFE 102 (contd)

Fig 116 (contd)

TAGTGA AATGGCGGTACAGACCTGGGTGTAGCTTGGGTTGATACCCAGATCGATACAGTCAATGAAGTG  
 OGTGAATGGTTCCGCCATTACCTAGAAATTGAAAATCAAAAGATTACCAGCTTGGTCAGGATGAAGCTT  
 ACAGAGGCATGGGAACCTACTTTGGAAGTCCTTGCTATTATTGATAATCAGGCTATCTATGCTCATATTGOT  
 GATTCCCGTATCGGCTTGATTCTGTGGAGAAGAATACCATCAGTTGACGAGCGATCATTCCTTGGTFAATG  
 AATTGCTCAAUGCTGCTCAATTGACACCAGAAGAGGCAGAAAGCTCATCCGCAAAAAAATATTATCAACC  
 AGTCTATTGGGCAAAAAGATGAAATTCAGCCTGATTTTGGGACAGTTATCCTTGAGTCAGGTGACTATCT  
 CTTCCTCAATAGTGACGGCTTGACCAACATGATTTACGGCAGTGAGATTCTGTGATATTGTAACCAAGTGAT  
 ATTCTTTAGCAGATAAAACGGAGACACTTGTTCTGTTTGTCTAACAAATGCAGGAGGTTTAGACAACATTA  
 CGTTGCCCTTCTTTCTATGAACGAGGAGGATGAAGAATCTGAGCACCACCACCACCACCACTGA

Fig 117

## 2 CFE103 "homologue of SEQ. ID NO. 99"

ATGACGATACAGATGAAGAATACAGGTAAACGAATTGATCTGATAGCCAATAGAAAACCGCAGAGTCAA  
 AGGGTTTGTATGAATTGCGAGATCGTTTGAAGAGAAATCAGTTTATACTCAATGATACCAATCCGGATA  
 TTGTCATTTCCATTTGGCGGGGATGGTATGCTCTTGTCGGGCTTTTATAAGTACGAAAATCAGCTTGACAA  
 GTCCGCTTATCGGCTTTCATCTACTGGACATTTGGGCTTCTATACAGATTATCGTGATTTGAGTTGACAA  
 GCTAGTGACTAATTGGCAACTAGATACTGGGGCAAGGGTTTCTTACCCTGTTCTGAATGTGAAGGTCTTTC  
 TTGAAAATGGTGAAATTAATTTTTCAGAGCACTCAACGAAGCCAGCATCCGAGGTCTGATCGAACCAT  
 GGTGGGAGATATTGTAATAAATGGTGTTCCTTTGAAAGCTTTTCGTGGAGACGGGGCTAACAGTTTTCGACA  
 CGGACTGGTAGTACTGCCTATAACAAGTCTCTTGGCGGTGCTGTTTACACCCTACCATTTGAAGCTTTGCA  
 ATTAACGGAGATTGCCAGCCTTAATAATCGTGTCTATCGAACATTGGGCTCTTCCATTATTGTGCTTAAGA  
 AGGATAAGATTGAACCTTATTCCAACAAGAAACGATTATCATACTATTTCGGTTGACAATAGCGTTTATTCT  
 TTCCGTAATATTGAGCGTATTGAGTATCAAAATCGACCATCATAAGATTCACTTTGTGCGGACTCCTAGCCA  
 TACCAGTTCTGGAACCGTGTTAAGGATGCCCTTATCGGTGAGGTGGATGAACTCGAGCACCACCACCAC  
 CACCACCTGA

Fig 118

## 2 CFE104 "homologue of SEQ. ID NO. 100"

ATGTCAAAAGAAATTAATTTTCATCAGATGCCGCTTCAGCCATGGTTTCGTGGTGTGATATCCTTGCA  
 ACACGTGTAAGTAACCTTGGGACCAAAAGGTGCGAATGTCGTTCTTGAAGATCATTCGGTTCAACCTT  
 GATTACCAATGACGGTGTGACCATTTGCCAAAGAAATCGAATTGGAAAGACCATTTTGAAGAAATATGGGTCT  
 AAGTTAGTATCAGAAAGTAGCTTCTAAAACCAATGATATCCAGGTGACGGGACTACGACTGCAACAGTCT  
 TGACCAAGCTATCGTCCGTGAAGGAATCAAAAACGTCACAGCAGGTGCAAAATCCAATCCGTATTGCTCG  
 TGGGATTGAAAACGAGTTGGCGCAGCAGTCGAAGCTTTTGAAGAAACCAACGCCATCCCTGTTGCCAATAA  
 AGAAGCTATCGCTCAAGTTGCGAGCCGTATCTTCTCGTTCTGAAAAAGTTGGTGAGTACATCTCTGAAGCA  
 ATGGAAAGAGTTGGCAAGACGGTGTATCACCATCGAAGAGTCAAGTGGTATGGAAACAGAGCTTGAA  
 GTGGTAGAAGGAATGCAGTTTGACCGTGGTTACCTTTCAAGTACATGGTGACTGATAGCGAAAAAATGG  
 TGGCTGACCTTGAAGAAATCCGTACATTTGATTACAGACAAGAAAAATTTCCAATATCCAAGAAATCTTGCC  
 ACTTTGAAAAGCATTCTCCAAAGCAATCGTCCACTCTTGAATTTGCGGATGATGTGGAATGCCAGGCT  
 CTTCCAACTCTTGTGTTTGAACAAGATTGCTGGAACCTTEAACGTAGTAGCAGTCAAGGCACCTGTTTTGG  
 TGACCGTCGCAAGCCATGCTTGAAGATATCGCCATCTTAACAGGGCGAAGCAGTTATCAGAGAAACCTT  
 GGTCTTGAGTTGAAAGATGCGACAAATTGAAGCTCTTGGTCAAGCAGCGAGAGTGACCGTGGACAAAGAT  
 AGGACCGTTATTGTAGAAGGTGCAGGAAATCCTGAAGCGATTCTCACCGTGTGCGGTTATCAAGTCTC  
 AAATGGAAACTACAACCTTCTGAATTTGACCGTGAAAAATTGCAAGAACGCTTGCCAAATTTGTCAGGTGG  
 TGTAGCGGTTATTAAGGTTGGAGCCGCAACTGAAACTGAGTTGAAAGAAATGAAACTCCGCAATTGAAGA  
 TGCCCTCAACGCTACTCGTGCACTGTTGAAGAAGGTATTGTTCCAGGTGGTGGAACAGCTCTTGCCAAT  
 GTGATTCCAGCTGTTGCTACCTTGGAAATTGACAGGAGATGAAGCAACAGGACGTAATATTGTTCTCGTG  
 CTTTGGAAGAACCCGTTCTGTCAAATTGCTCACAATGCAGGATTGGAAGGATCTATCGTTATCGATCGTTTG  
 AAAAATGCTGAGCTTGGTATAGGATTAAACGCAGCAACTGGCGAGTGGGTAAACATGATTAATCAAGGT  
 ATCATTGATCCAGTTAAAGTGAATCGTTGAGCCCTACAAAAATGCAGCATCTGTAGCCAGCTTGATTTTGA  
 CAACAGAGCAAGTCGTAGCCAAATAACCAAGAACCAAGTACCCAGCTCCAGCAATGGATCCAAGTATGA  
 TGGGGGATGATGCTCGAGCACCACCACCACCACCACTGA

Fig 119

## 2 CFE105 "homologue of SEQ. ID NO. 101"

ATGATTAAAGATTGAAACCGTATTAGATATTTTAAAGAAAGATGGCCTTTTTCGCGAAATTTGACCAAG  
 GTCATTACCACTACAACCTACAGCAAGTTATTTTGTATGATCAGTACGACAGCCGAAAAAGTAACAGA  
 AGACACTCTTTTTCGCAAAAGCGCTGCTTTTAAAAAAGAAATACCTTCTTCTGCTATAACACAAGOTT  
 TAGCTTGATATGATGCTGAAAAGGACTACGAAGTCATATCCCTGTCTCATTGTGAACGATATAAAGAA

2 CFE 105 homologue of SEQ ID NO: 101 (Contd)

Fig. 119 (Contd)

AGCCATGAGTTTGATTGCCATGGAGTTCTATGGTAATCCACAAGAGAACTCAAACCTCTTGCCCTTTACT  
GGTACTAAGGGTAAGACAACAGCAACCTATTTCGCCTATAACATCTTATCTCAAGGGCATAGACCTGCTA  
TGTGTGACCATGAACACAACCTCTTGATGGCGAGACTTTCTTTAAGTCAGCGTTGACAACCCCTGAGAG  
TATGACCTCTTTGACATGATGAATCAGGCTGTGCAAAATGACCGTACCCACCTCATCATGGAAGTCTCC  
AGTCAAGCCTATCTAGTCCATCGAGTCTATGGACTGACCTTTGATGTAGGAGTCTTTCTTAACATCACTCC  
TGACCATATCGGCCGATTGAACACCCCTAGCTTTGAAGACTATTTCTACCACAAGCGTCTCTTGTATGGAA  
AATAGCGGAGCAGTCATTAACAGTGACATGGACCACTTCTCAGTCTTGAAAAGAACAGGTTGAAGATC  
AAGACCATGATTTCTATGGTAGCCAATTTGATAACCAAAATCGAGAATTCCAAAGCCTTTAGCTTTTCAGCT  
ACCGGTAAACTCGCTGGAGATTATGATATCCAACCTATTGCAACTTCAACCAAGAAAATGCAGTTGCTG  
CTGGACTGCTTGTCTCCGTCTCGGAGCAAGTCTTGAGGACATCAAAAAAGGCATCGCTGCAACCCCGGT  
TCCTGGTCGTATGGAAAGTCCCTCACTCAGAAAAATGGAGCCAAGGTCTTCATCGACTATGCCACAATGGG  
GATAGTCTGAAAAAACTCATCAATGTGGTTGAAACTCATCAAAACCGGAAAGATTGCTCTGGTTCTGGGAT  
CAACAGAAAAAAGGGAGAAAGTCGTGTAAGGACTTTGGCCTCTCTCTCAATCAACACCCCTGAGATTCT  
AAGTCTTCTGACTGCTGATGACCTAACTATGAAGCCAAATGGCCATTGCGAGTGAAATTAGTAGCTA  
CATCAATCATCTGTTGAAAAAGATTGCGGATCGCCAAGAACCCATCAAGGCGGCAATGGCTATCAGAAA  
TCACGAATTAGATGCAGTTATTATTGCGGGTAAGGGAGCGGATTGTTACCAAAATCATCCAGGGCAAGAAA  
GAATCTACCCAGGAGATACAGCCGTGCGAGAAAATTATTACTCGAGCACCACCACCACCACCTGA

2 CFE 106 "homologue of SEQ. ID NO. 102"

Fig. 120

ATGATCCAAATCGGCAAGATTTTGGCGGACGCTATCGGATTGTCAAACAGATTGGTTCGAGGAGGCATGG  
CGGATGTACTACCTAGCCAAAGACTTAATCTTAGATGGGGAAGAAAGTGGCAGTGAAGGTTCTGAGGACCA  
ACTACCAAGACCGGACCGATAGCTGTAGCTCGTTTTACGCGTGAAGCGAGAGCTATGGCAGATCTAGACCA  
TCCTGATATCGTTCCGGATAACAGATATTGGTGAGGAAAGACGGTCAACAGTATCTTGCAATGGAGTATGTT  
GCTGGACTAGACCTCAAACGCTATATCAAGGAACATTATCCCTTTCTAATGAAGAAGCAGTCCGTATCA  
TGGACAAATTTCTTTGGCTATGCGCTTGGCCATACTCGAGGAAATGTTTCACAGGGACTTGAAACCTCA  
AAATATGCTTTTGACACCAGATGGGACTGCCAAGGTCAACAGACTTTGGGATTGCTGTAGCCTTTGCAGAG  
ACAAGTCTGACCCAGACTAACTCGATGTTGGGCTCAGTTCACTTGTGTCACCAGAGCAGGCGCGTGGTT  
CGAAGGCGACTGTGACAGAGTGATATCTATGCCATGGGGATTATTTCTATGAGATGTTGACAGGCTAT  
CCCTTATGACGGGGATAGCGCGGTGACCAATTGCCCTCCAGCATTTCAGAGAACCCCTGCCGTCCGTTATTO  
CAGAAAATTCATCTGTACCTCAGGCTTTAGAAAAATGTTATTATCAAGGCAACTGCTAAAAAGKTOACCA  
TGGCTATCGCTCGGTTTCAGAGATGATGTAGACTTGTTCTAGTACTTCTCTACAATCGTAGAAATGAAA  
GTAAGTTAATGTTGATGAAAAGGCAAGGCGAGATACCAAGACCTTGCCGAAGGTTTCTCAGAGTACCTT  
GAGATCTATTCTTAAGGTTCAAGCGCAGACAGAACCAAAATCAATCAAAAAACCAAGCGGCTGTGAC  
AAGGAAACTTACCAACCACAAGCACCGAAAAAACATAGATTTAAGATGCGTTACCTGATTTTGTGGCC  
AGCCTTGATTGTTGGCAGCTTCTCTTATTGGATACTATCCAGAACTCTTGCAACCATTGCCATTCCAGA  
TGTGGCAGGTCAGACAGTTGACAGGCGCAAGGCAACGCTCAAAAAAGCCAAATTTGAGATTGTTGAGGA  
GAAGACAGAGGCTAGTGAAAAGGTGGAAGAAGGGCGGATTATCCGTACAGATCTCTGGCGCTGGAAGTGG  
TCGAAAAGAAAGGAACGAAAATTAATCTGGTTGTCTCATCAGGCAAAACATCTCTCAAATTAAGTAAT  
GTGGCGGGAATCTTCTGATGTTATCGCGGAATTAAGAGAGAAAAAGTTCCAGATAATTTGATTAAAA  
TTGAGGAAGAAAGAGTCGAATGAAAGTGAGGCTGGAACGGTCTGAAAGCAAAGTCTACCAGAAGGTACG  
ACCTATGACTTGAGCAAGGCAACTCAAAATGTTTGGACAGTAGCTAAAAAAGCTACGACGATTCAATTAG  
GGAAGTATATTGGACGGAAGCTCTACAGAAAGTAATCTCAGAACTCAAGCAGAAAGAGGTTCTGAGAATT  
TGATTAAGATAGAGGAAGAAGAGTCCAGCGAAAGCGAAACGATTATGAAACAAAGTCCAGGT  
GCCGGAACCACTTATGATGTGAGTAAACCTACTCAAAATTTGCTTTCAGAGTAGCTAAAAAAGTTACAAGTG  
TTCCATGCCGAGTTACATTTGTTCCAGCTTGGAGTTTACTAAGAACAATTTGATTCAAAATTTGTTGGGATT  
AAGGAAOCTAATATAGAAGTTGTAGAAGTGACGACAGCGCTGCAGGTAGTGTAGAAGGCATGGTTGTT  
GAACAAAGTCTAGAGCAGGTGAAAAGGTAGACCTAAATAAGACTAGAGTCAAGATTTCATCTACAAA  
CCTAAAACAACTTCAGCTACTCTGCGGCGCACTGAGCAACACCACCACCACCTGA

2 CFE 107 "homologue of SEQ. ID NO. 103"

Fig. 121

ATGAAACATTTGATACTATTTCATCGGTGGGGACCTGCTGGTATGATGGCTACGATTTCCAGTAGCTT  
TTATGGACAGAAAACCCCTCTCATCGAAAAAATCGGAAACTTGGAAAAAATAGCTGGGACTGOTGG  
GGGACGTTGCAATGTGACCAACAATGGTAGCTTAGACAACCTGCTAGCTGGAATTCCTGGAACCGGACG  
CTTTCTTACAGTGTCTTCTCCAGTTGATAATCTGATGACATCAACTTTTTTACAGAAAAATGGTGTAA  
ACTTAAGGTGGAAGACCAAGGACGCGTCTTCCAGCGGACAAAGTCTCGGACTATTATCGAAGCTTTG  
GAAAAGAAAACTACTGAAGTGGTCAAGTTGCTACTCAAAATAGAAATCGTTTCTGTTAAAAAAGTA

## 2CFE 107 (contd)

Fig 121 (contd)

GATGACCAAGTTTGTCTTAAGTCAACGGATCAAACCTTCACTTGTAAAGAACTCATTGTCAACAACAGGTG  
 GTAGTCTTATCCTTCGACTGGTTCCACTGGCTTTGGTCACGAGATTGCTCGCCATTTTAAGCATACCATC  
 ACCGATCTTGAAGGCTGCTGAAAGTCCCTTTATTAACAGATTTTCCACATAAAGCCTTACAAGGGATTCTCT  
 GGACGATGTGACCCTAAGTTATGGTAAGCATGTCATCACTCATGATTACTCTTTACCCACTTTGGTTGT  
 CAGGTCTGCTGCCCTACGCATGTCTAGCTTTGTCAAAGGTGGGGAGGTTCTCTCACTCGATGTTTTGCCCT  
 CACTTTCTGAGAAGGACTTGGTTACATTTCTAGAAGAAAAATCGGGAAAAATCCTTGAAAAACGCTTTAA  
 AAACCTTGTACAGAACGCTTGGCCGAATTTTTGTACAAGGATATCCTGAAAAAGTCAAACAGCTGAC  
 TGAAAAAGGAACGGAACAACCTTGTCCAGTCCATTAAAGAACTTAAATTCCTGTAACTGGAAAAATGTC  
 CCTTGCAAAGTCCCTTTGTTACCAAGGGTGGAGTCACTCTCAAGGAAATCAATCCTAAACCCCTTGAAAGT  
 AAGCTGTACCTGGCCTCCACTTTGCAGGCGAAGTTATGGATATCAATGCCACACGGGTGGCTTTAACA  
 TCACTTCTGCCCTCTGTACCGGCTGGGTGGCGGGAAGTCTGCATTATGATCTCGAGCACCACCAACCA  
 CCACTGA

Fig 122

## 2 CFE108 "homologue of SEQ. ID NO. 104"

ATGCTGAAATGGGAAGACTTGCCTGTGGAAATGAAATCAAGCGAGGTTGAGTCTTACTACCAGCTTGTCT  
 CTAAGGGAAGGGTTGCTGATTTCAAGCGTTGCTTGGACTGGGTTTGGCCTTGGTCTTACTGGTTCTA  
 ACTCTCTCCATCTTTCTCATCTTGAGCATTTGGATCAAGTTGGATAGCAAGGGGCCAGTGATTTACAAGCA  
 AGAGCGTGTGACCCAGTACAACCGTCCGTTCAAGATTTGGAAGTTCGGTACCATGGTGACGGATGCGGAT  
 AAAAAAGGAAGTCTGGTGACTTCTGCTAACGATAGCCGATTACCAAGGTTGGAAATTTTCATCCGACGTG  
 TCGTTTGGACGAAGTGCCTCAATGGTCAATGTCTTAAAGGTGAGATGTCTTTGTCTGGTACACGACCT  
 GAAGTGCCACGTTATACAGAGCAGTATAGCCCTGAAATGATGGCAACCTTGTCTTGAAGCAGGAATTA  
 CCTCTCCAGCCAGCATCAACTACAAGGATGAGGACACCATCATCAGTCAAATGACGGAGAAAGGTCTGT  
 CAATTGATCAGGCCTATGTGGAGCATGTTCTTCTGAAAGATGCGCTATAACCTCGCCTATCTCCGAGA  
 GTTAGTTCTTTGGGGACATCAAAATCATGTTTCAAACCGTGTGTTGAGGTACTAAACTCGAGCACCACC  
 ACCACCACTGA

Fig 123

## 2 CFE109 "homologue of SEQ. ID NO. 105"

ATGACTAGTCCACTATTAGAATCTAGACGCCAACCCGTAATGCGCTTTTCAAGCTCTCATGAGCCTTGA  
 GTTCGGTACGGATGTGCAAACTGCTTGTGCTTTCGCTATACTCATGATCGTGAAGATACGGATGTACAA  
 CTCCAGCCTTTTGTATAGACCTCCTTCTGTGTTCAAGCTAAAAAGGAAGAACTAGATAAGCAAAATCA  
 CTGAGCATTTAAAGCAGGTTGGACCATTTGAACCGTTAAACGCTCGTGGAGAGAAACCTCTTCGCTTGGG  
 AGTCTTTGAAATCACTTCATTGACACTCCTCAGCTGGTTGCTGTTAATGAAGCTATCGAGCTTGCAGAGG  
 ACTTCTCCGATCAAAAACTGCCCGTTTTATCAATGGACTGCTCAGCCAGTTTGTAACAGAAAGAACT  
 CGAGCACCACCACCACCACCACTGA

Fig 124

## 2 CFE111 "homologue of SEQ. ID NO. 107"

ATGACAAAACGTGTAAACGATTATTGATGTAAAAAGACTATGTTGGTCAAGGAAGTGACGATTGGCGCTTGGG  
 TTGCCAACAAATCAGGAAAAGGGAATCGCTTCTTACAATTGCGTGATGGAACAGCCTTCTTCAAGG  
 TGTGACTTTTAACCAAACCTTTGTGCAAAAAATTTGGTGAAGAAAGTGGGACTTGAGAAGTTTGATGTTATC  
 AAAACGCTTGAGCCAAGAAACGCTCTGTTTATGTGACAGGTATTGTCAAAGAGGACGAACGTTCTAAATTTG  
 GCTATGAGTTGGACATCACAGACATCGAAGTGATCGGTGAATCTCAAAGACTACCCAATCACACCAAAAG  
 AAGACGGAACAGACTTTTGTATGGATAACCGTCACTTGTGGTACGCTCTGTAAAGCAAGTAGCTGTGTT  
 GCAAAATCGTAACGCTATTATCTATGTAACCTTATGAGTTCTTTGACAAGAATGGTTTTATGAAGTTTGACA  
 GCCCAATCTTTTCAGGAAATGCGGCAGAAAGATTCTACAGAACTCTTTGAAACTGACTACTTCGGAACGCC  
 AGGCTACTTGAGCCAATCAGGTCAGCTTTACCTAGAAAGCAGGGGCTATGGCTCTTGGTCTGTCTTGA  
 TTGTTCCAGTTTTCGCTGCTGAAAAATCAAAAAACCGCGTCACTTGACTGAGTTCTGGATGATGGATGC  
 TGAGTACTCATCTTGACACATGATGAGTCTGCTTGAAGAAAGCTTATGTGAAAGCTCTTCTACAA  
 GGTGTTCTTGACCGCGCGCTCAAGCCTTGGAAACCTTGGAAACGCTGATACAGAACTCTTGAAACGCTACA  
 TTGCAAGGCCATTCAAACGTATCATTACGATCAAGCCATTGACCTCTTGCAAGAGCATGAAAAATGATGA  
 AGATGCTGACTACGAGCATCTTGAGCATGGTGATGACTTTGGGTCAACACAGAAACTTGGATTTCAAAC  
 CACTTTGTTGTGCCAACATTTGTCATGAACATCCAGCAGCCATCAAGGCCTTCTACATGAAACCAAGTTCC  
 TGGAAATCCAGAGCGCGTGCTTTGTGACAGACTTGCTTGTCTCAGAAAGGCTATGGAGAAATTATCGGTGGG  
 TCTATGCTGAGGAAGATTACGATGCCCTTGTGCTAAGATGGATGAACTTGGCATGGATCGTACAGAAT  
 ATGAATTTACCTTGACCTTCGFAAATACGGTACAGTTCCACACGGAGGATTGGTATCGGTATCGAAGG  
 TATGGTAACCTTCGAGCAGGAACAAAAATATCCGTTGAAGCTATTTCAATCCACGATGTTGACCCGT  
 ATCAAACCACTGAGCACCACCACCACCACCACTGA

## 2 CFE112 "homologue of SEQ. ID NO. 108"

ATGCTCAAAAATTAGTAGAAATCAAAGATTAGAAAATTCCTTCGGTGAAGGAAGTAAGAAGTTTGTGG  
 CGTTTAAAAATGCTAACTTCCTTATCAACAAGGGAGAACTTTCTCGCTTGTAGGTGAGTCCGGTAGTGG  
 GAAAAGCAACTATTGGTCTGCTATCATCGGTCTAAATGATACAAGTAATGGAGATATCATTTTTGTAGGT  
 CAAAAGATTAATGOTAAGAAATCGCGTGAACAAGCTGCGGAATTGATTCTGTCGAATCCAGATGATTTTCC  
 AAGACCTGCGCGCAAGTTTGAATGAACGTGCGACTGTTGATTATATTATTTCTGAAGGTCTTTACAATCAC  
 CGTTTATTTAAGGATGAAGAAGAACGTAAAGAGAAAGTTCAAAGTATTATCCGTGAAGTAGGTCTTCTTG  
 CTGAGCACTTGACTCGTTACCTCATGAATTCTCAGGCGGTCAACGTCAACGTATCGGTATTGCCCGTGCC  
 TTGGTCTGCAACCAGACTTTGTTATTGCAGATGAGCCAATTTACGCCCTTGGACGTTTCTGTACGTGCCA  
 AGTTCTTCAACTTGCTCAAAAAATTCAAAAAGAGCTCGGCTTGACCTATCTCTTCATCGCCCATGACTTGT  
 CGTTTGTTCGCTTATTTAGATCGTATCGCAGTTATTACAAGGGTGTATTGTAGAGGTGTCAGAAACA  
 GAAGAATTGTTTAAACAATCCAATTCACCCATATACTCAAGCCTTGCTTTCAGCGGTACCAATCCAGATCC  
 AATCTTTCGAAGCTAAGAAGGTCTTGAAGGTTTACGACCCAAGTCAACACGACTATGAGACTGATAAGCC  
 ATGTATCGTAGAAATCCGTCCAGGTCACTATGTTTGGGCGAACCAAGCTGAATTAGCACGTTATCAAAAA  
 GGACTAAACCTCGAGCACCAACCACCACCACCACTGA

## 2 CFE113 "homologue of SEQ. ID NO. 109"

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 ATCCAGCAAGGCCACATGAAACTACAGGCCAAATCCCTAGCTCTCTAGCTGGGGCTAGTGAATCTGAAG  
 TTGCTCCCTAGTAGAGCGCCTCATCTCAGATAAAACCTTAACTAGAGACAGCCAGCCCTATCTCGA  
 AAATTTAAGATCAGCGGCCGCACTCGAGCACCAACCACCACCACCACTGA

## 2 CFE114 "homologue of SEQ. ID NO. 110"

ATGCCAATTACATCATTAGAAATAAAGGACAAGACTTTTGAAATCGATTCAAGAGGTTTGTATCCAGAAO  
 AAGTCGATGAATTTTATGATATTGTGGTTCTGTGATTACGAAGATCTTGTGCGTGCGAATCATGATAAAAA  
 TTTGCGTATTAAGAGTTTAGAAGAGCGTTTGTCTTACTTTGATGAAATAAAGATTCAATTGAGCCAGTCTO  
 TATTGATTGCTGAGGATACAGCTGAGAGAGTGAACAGGCGGCGCATGAACGTTCAAAACAATATCATTC  
 ATCAAGCAGAGCAAGATGCGCAACGCTTGTGGAAGAAGCTAAATATAAGGCAACCAAGATTCTTCGTC  
 AAGCAAGTGATAATGCTAAGAAAGTCGCTGTTGAAAACAGAAGAATTGAAGAACAAGAGCCGTGCTTCC  
 ACCAACCCTCTCAAACTACAAATGAGAGTCAGTTGGCTATTGTTGAATCTTCAGATTGGGAAGATATTCTC  
 CGTCCAAAGCTACTTATCTTCAAAACAGTGATGAAGCCTTAAAGAAAGTGTTAGCGAAGTACTTGGAG  
 AACCGATTCCAGCTCCAATTGAAGAAGAACCAATTGATATGACACGTCAGTTCTCTCAAGCAGAAATGGA  
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 AGTGGAAACTCCAACCTCCTGTAGTGAGTCCCTCAAGTTGAAGAAGAGCCCTCTGCTCATCCAGTTGGCCAA  
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## 2 CFE115 "homologue of SEQ. ID NO. 111"

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 AATCTTCTACGTAAGCGAAACGAGGGGAGATTAGAGGCGCTAGAAGAAAGAAAAAGAACTATACA  
 ATCTTCCAGTAATGATGAAGTAGAAGCTGTAAAAATATGCACCTTGATTGGACAAAGTCAAGTGGCTTT



2CFE 115 (Contd.)

Fig 128 (Contd.)

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## 2 CFE116 "homologue of SEQ. ID NO. 112"

Fig 129

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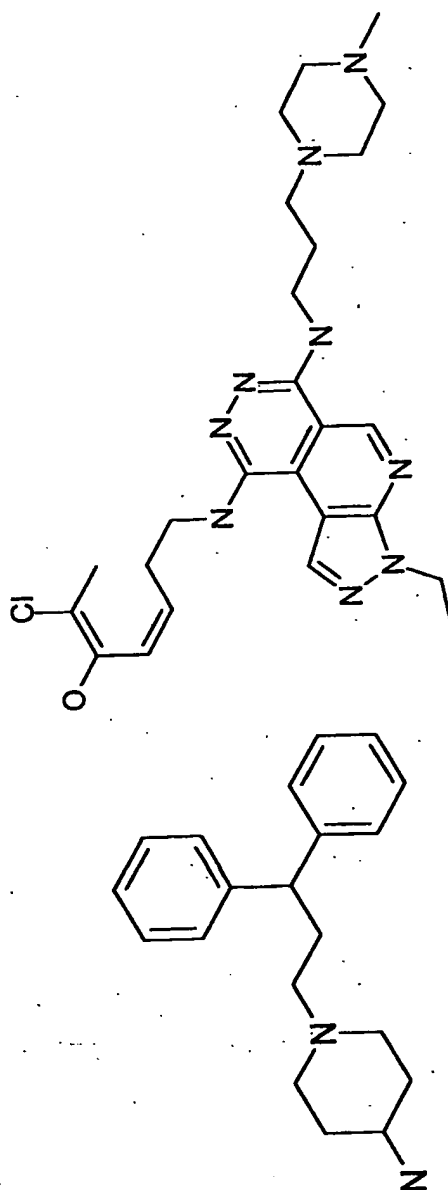
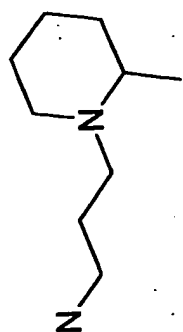
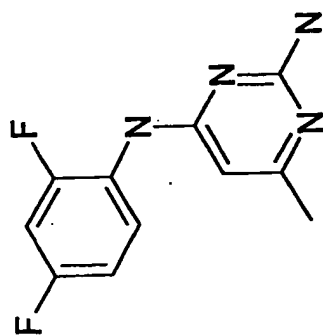
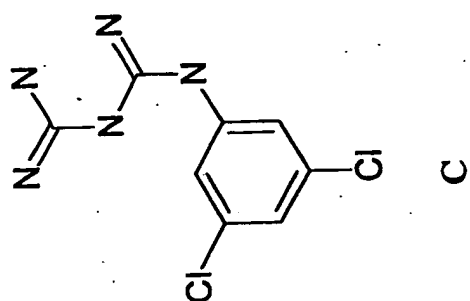
2CE 116 (contd)

Fig 129  
(contd)

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Fig 130

2 CFE117 "homologue of SEQ. ID NO. 113"  
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**E**

**FIGURE 131**

## SEQUENCE LISTING

- <110> Dougherty, Thomas J.  
Pucci, Michael J.  
5 Dougherty, Brian A.  
Davison, Daniel B.  
Bruccoleri, Robert E.  
Thanassi, Jane A.
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&lt;210&gt; 21

&lt;211&gt; 519

30 &lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 21

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&lt;210&gt; 22

45 &lt;211&gt; 720

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 22

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5

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<211> 732

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<211> 831

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<213> Streptococcus pneumoniae

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 <211> 483

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 38

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 taa 483

15 &lt;210&gt; 39

&lt;211&gt; 570

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

20 &lt;400&gt; 39

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 aatgttggtt ttatgttgat tgatcaacta gcgaagaaac agaattgtcac ttttacacac 120  
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 gttaaaccaa cgacctttat gaatgaaagt ggaaaagcag ttcattgcttt attaaacttac 240  
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 30 gagaaaacaa tgcagaggta taacggataa 570

&lt;210&gt; 40

&lt;211&gt; 852

&lt;212&gt; DNA

35 &lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 40

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 40 atggttgaga aagtttttga agaggtgaaa ccgactttag tctaccattg tgcagcctac 180  
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 45 catgtgtcta atttctatat tatccgtact gcttgggtat ttggaaatta tggcaaaaac 480  
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 50 agtcaatttc cagccaaagc taaacgtccg ctaaactcaa cgatgagcct ggccaaagcc 780  
 aaagctactg gatttggtat tccaacttgg caagatgcat tgcaagaatt ttacaaacaa 840  
 gaagtggat aa 852

&lt;210&gt; 41

55 &lt;211&gt; 1224

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

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 <212> DNA  
 <213> Streptococcus pneumoniae

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 35 gagcaaaaat ggtctaata aattcaaggg gagattatcc gtgaggaact ggctactttg 300  
 agagaacagt tggctcagac agaagagatt ttcttcattg atattcccct actttttgaa 360  
 caggactaca gcgattggtt tgctgagact tggttggtct atgtggaccg agatgcccaa 420  
 gtagaacgct taatgaaaag ggaccagttg tccaaagatg aagctgagtc tcgtatggca 480  
 gccagtggtc ctttagaaaa aaagaaagat ttggccagcc aggttcttga taataatggc 540  
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<210> 43  
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 5 atactcttag ctgctgcagt tggtaaagga attcgtataa ataatgttct ttacgaacac 780  
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 25 ttgattgata aaattcatga tgcagggtct aaggctggtg ttgtccttaa tcctgaaaca 360  
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 <212> DNA  
 5 <213> *Streptococcus pneumoniae*  
  
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 10 atagctgagg agtttgggtg tagtcgctcag gctgtctatg acaatatcaa gcgaacagaa 180  
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 35 <213> Streptococcus pneumoniae  
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 <211> 1809

&lt;212&gt; DNA

213&gt; Streptococcus pneumoniae

&lt;400&gt; 56

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35 gtagaataa 1809

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&lt;210&gt; 57

&lt;211&gt; 723

&lt;212&gt; DNA

40 &lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 57

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&lt;210&gt; 58



&lt;211&gt; 2223

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

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45 &lt;210&gt; 59

&lt;211&gt; 1479

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

50 &lt;400&gt; 59

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|    |                                |            |             |            |            |            |      |
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|    | agtgaaaatc                     | ttgttactgc | tcctgtgggt  | acggatcttg | caacggctga | gagtattctt | 540  |
|    | caagagcatc                     | gtattgaaaa | acttcggtt   | gtcgatgaag | aaggcagctc | ttctgggttg | 600  |
|    | atcactatca                     | aagatattga | aaaagttatt  | gagtttccaa | atgcggtcaa | agatgagttt | 660  |
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|    | aaaggttcaa                     | gcgaccgtta | tttccaaggt  | tctgtcaatg | aagcaaaca  | gcttggtcca | 1260 |
| 15 | gaaggaattg                     | aaggtcgtgt | tgcttataaa  | ggagcggcag | ctgatattgt | tttccaaatg | 1320 |
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|    | gataatgctc                     | aatttattga | aatgtctggt  | gctggtttga | aagaaagcca | tcctcatgat | 1440 |
|    | gtgcaaatga                     | ctaagtaggc | accaaattat  | tctatgtaa  |            |            | 1479 |
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|    | ttagagggtc                     | tagaggctgt | tcgtatgcgt  | ccagggtatg | acattggatc | aacctcaaaa | 120  |
|    | gaaggtcttc                     | accatctagt | ctgggaaatt  | gttgataact | caattgacga | ggccttgga  | 180  |
|    | ggatttgcca                     | gccatattca | agtttttatt  | gagccagatg | attcgattac | tggttggtg  | 240  |
| 30 | gatgggctgt                     | gtatcccagt | cgatattcag  | gaaaaaacag | gccgtcctgc | tggtgagacc | 300  |
|    | gtctttacag                     | tccttcacgc | tgtaggaaag  | ttcggcgggt | gtggatacaa | ggtttcaggt | 360  |
|    | ggctttcacg                     | gggtggggtc | gtcagtagtt  | aatgcccttt | ccactcaatt | agacgttcat | 420  |
|    | gttcacaaaa                     | atggtaagat | tcattaccaa  | gaataccgtc | gtggtcatgt | tgtagcagat | 480  |
|    | cttgaaatag                     | ttggagatac | ggataaaaaca | ggaacaactg | ttcacttcac | accggacca  | 540  |
| 35 | aaaatcttca                     | ctgaaacaac | aatctttgat  | tttgataaat | taaataaacg | gattcaagag | 600  |
|    | ttggcctttc                     | taaatcgcg  | tcttcaaatt  | tcaattacag | ataagcgcca | aggtttgga  | 660  |
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|    | gttgaggtag                     | ccatgcagta | caacaactgt  | taccatgaaa | atgtcatgag | tttcgccaat | 840  |
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|    | caagaaatca                     | aactccaaga | agcttttagc  | cgttatagtg | aaggtcgtac | caaaccgact | 1740 |
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|    | gatcccgaac                     | atcgcttgat | ggctagagtt  | tctgtagatg | atgctgcaga | agcagataaa | 1860 |
|    | atctttgata                     | tggtgatggg | ggatcgagta  | gagcctcgtc | gtgagtttat | cgaagaaaat | 1920 |

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 caaatcgtag gttacgtatt gagtggagac cctgcctacg ttcctcgta taataatgca 180  
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15 <210> 62  
 <211> 597  
 <212> DNA  
 <213> Streptococcus pneumoniae

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 35 <213> Streptococcus pneumoniae

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 cttccaacta ttaagtacat catcgaacaa ggtggacgtg caattctttt ctctcacctt 180  
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 ggtaactcac ttgtagaaga agacaaattg gatgttgaga aagctcttct tgaaaaagca 780  
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 gctatcgtga aacaaccagg agttaaatc atcatcggtg gtggtgactc agctgccgca 1080  
 35 gcatattaac ttggcgtgc agacaagttc tcatggatta gtacgggtg tggagcatca 1140  
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 <211> 498  
 40 <212> DNA  
 <213> Streptococcus pneumoniae  
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 cgttttccta ataccgtatt tgcaggcttt tatttgttcg atggaagga attggtttta 180  
 ggcccttcc aaggaggtgt ttctgcac cgtattgcac taggcaaggg tgtttgtggt 240  
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 50 ttacttggag ttctggatct ggattcttca gagattgagg attacgatgc tatggatcga 420  
 gattatttgg aacaatttgt cgctattttg cttgaaaaga cagcatggga ctttacgatg 480  
 tttgaggaaa aatcttaa 498  
 <210> 67  
 55 <211> 630  
 <212> DNA  
 <213> Streptococcus pneumoniae

<400> 67  
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 aaaaaacgca aacaagttgg gatttttaggg gggaatttta accctgttca caatgcccat 120  
 5 ctcaattgtt cggatcaagt acggcaacag ttgggactgg atcaagttct gctcatgcct 180  
 gaataccaac ctccctcacgt tgataaaaag gaaaccatcc ctgaacacca tcgtctcaag 240  
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 10 attgatgaac tggttgacat ggttcagttt gtgggggttc agcgtccacg ctacaaggta 480  
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15 <210> 68  
 <211> 768  
 <212> DNA  
 <213> Streptococcus pneumoniae

20 <400> 68  
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 tttgcgacag gcatttttga tgaatttatc caattacatg gtgaccgttc ttttcgtgat 120  
 gatggtgcag ttgttggtgg tattggttgg cttggagacc aagctgtaac agtgggttgt 180  
 atccaaaaag gcaagagttt gcaagacaac ctcaaacgga attttggcca accacatcca 240  
 25 gaaggctacc gaaaggcact gcggttgatg aaacaggctg agaaatttgg ccgtccagtt 300  
 gtgaccttta tcaatacagc aggtgcttat cctggtgtcg gagcggaaga acgtggtcaa 360  
 ggggaagcta ttgctcgcaa tctcatggaa atgagtgacc tgaaagttcc tattatcgcc 420  
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 tggatgctgg aaaattctat ctatgccatt ctacgtccag aaggctttgc ttccatttta 540  
 30 tgggaaggacg gtactcgcgc catggaagca gcagaactga tgaaaatcac ttcgcatgaa 600  
 ctgttagaaa tggacgtggt ggataagggtg atttctgaag taggactttc tagtaagaa 660  
 ctgattaaga gtgtcaaaaa agaactccaa acggagctgg ctagactttc acaaaaaccg 720  
 ctagaagagt tgctggaaga acgctatcaa cgatttagaa aataactaa 768

35 <210> 69  
 <211> 510  
 <212> DNA  
 <213> Streptococcus pneumoniae

40 <400> 69  
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 gcttatagtc tgaaaacttt gtcaactgag ttgggaaatc ctgactctga aacctatttc 180  
 attatgcatg aggaggagat agctgggttt ctcaaagtca actggggaag tgctcaaact 240  
 45 gagagagaat tagaggacgc ttttgaaatt caacgcctct atgtgctaca aaaattccaa 300  
 ggatttggac taggtaagca actgtttgaa ttcgcacttg aacttgctac aaaaaatagt 360  
 ttttcttggg ctgggctagg tgtttgggag catatataca aagctcaagc cttttataat 420  
 cgatatggtt ttgaaaaatt tagccaacat cattttatgg ttggtcaaaa agtagatacg 480  
 gattggttac tgagaaagaa attaaaggtaa 510

50 <210> 70  
 <211> 1590  
 <212> DNA  
 <213> Streptococcus pneumoniae

55 <400> 70  
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gtttacatta tcccttggtg catctggatg ggggcttatg cagctaaggc aaatggcttc 120  
 tttaccatgg gttacactat ctatgcttgg ttcttgttgg tttcaacagc ggggattcca 180  
 gttgcggtgg ccaagcaagt tgccaagtat aataccatgc gagaagaaga gcatagcttt 240  
 gccctgattc ggagcttctt aggcctttatg acaggactag gcctgggttt tgcttttagtc 300  
 5 ttgtatgtct ttgctccttg gctagcagac ttgtctggcg tgggcaaaga cttgatcca 360  
 atcatgcaaa gcttggcttg gggagtcttg attttcccg ctatgagtgt tatccgagga 420  
 tttttccaag ggatgaataa cctcaaacc tatgccatga gccaaattgc tgagcaggtc 480  
 attcgtgtta tctggatgct cctagcaacc tttatcatta tgaagctcg ttcaggagat 540  
 tatctagcag ccgttaccca atcaaccttt gctgcctttg tcggtatggt agccagtttt 600  
 10 gcagtcttga tttatttcct tgcccaagaa agttcactca aaagagtctt tgaaacagga 660  
 gataagatta acagtaagcg tctcttgggt gataccatta aggaagccat tccttttatc 720  
 ctgacagggg ctgccatcca gatcttcag attttggatc agctgacctt tatcaatagt 780  
 atgagctggt ttaccaacta cagcaatgag gacttgggtg tcatgttttc ttatttctca 840  
 gccaatccta ataaaatcac gatgattttg atttctgtag gggtttcgat tgggagtgtt 900  
 15 ggtttgccac ttttgacgga aaactatgct aagggggact tgaaagcggc ttctcgtctc 960  
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 atgcttcagg ccatgttccg caaccgcaag gccgttctct attttatcta tggttctatt 1200  
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 tcaacaacca ttgctctcat cattcctaac gtcttgatgt atcgggatat ttgtaaagta 1320  
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 ggagctttgt ggagcttctt ttatgtagct cttgtcgggt ccatgggggg tggactttat 1500  
 25 atggttatga gtctgcgtac ctatttatta gataaggtaa taggaaaagc ccaagcagat 1560  
 cgctgcgag caaaatttaa gctttcgtaa 1590

<210> 71  
 <211> 468  
 30 <212> DNA  
 <213> Streptococcus pneumoniae

<400> 71  
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 gatatcattg aacgggcgag cagactcttt gataagctct atgtcggtat tttttttaat 120  
 ccccaaaaac aaggatttct tcctatcgaa aatcgtaaac gggggctaga aaaggctttg 180  
 ggacatctgg aaaatgttga agtcgtggct tctcatgatg aattgggtgt cgatgttgca 240  
 aaaagattgg gtgctacttg tctagtgcgt ggtttgagga atgcgtcgga tttgcaatat 300  
 40 gaagccagtt ttgattacta caatcatcag ctgtcttctg atatagagac tatttattta 360  
 catagtcgac ctgaacatct ctatatcagt tcatcaggcg ttagagagct tttgaagttt 420  
 ggtcaggata ttgcctgcta tgttcccag agtatttga ggaaataa 468

<210> 72  
 <211> 432  
 45 <212> DNA  
 <213> Streptococcus pneumoniae

<400> 72  
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 aaacctatc aaacagctaa aagtgaagga gaaaaattag ctcagcagta tgcaggatta 120  
 gagcaggccg atcaggttga tttatacaat ggcttggaat cttattacag cgttcttgggt 180  
 cgtaataaac agcaagaagc acttgcgtgt ctgattggaa aagatgatca taagatttac 240  
 gtttatcagc taaatcaggg tgtttcacia gaaaaagcag aaacggtttc taaggaaaag 300  
 ggagctggcg aaattgacaa gattatcttt ggtcgttatc aagataagcc aatctgggaa 360  
 55 gtcaagtcag gatctgattt ttatctagta gattttgaaa caggagcatt ggtcaacaag 420  
 gagggcctat ga 432

<210> 73  
 <211> 732  
 <212> DNA  
 <213> Streptococcus pneumoniae

5

<400> 73  
 atgattgata ttcattcgca cattgtcttt gatgtagatg atgggcccaa gtcaagagag 60  
 gaaagtaagg ctctcttgac agaagcctac aggcaggggg tgcgaacat tgtctctacc 120  
 tctcaccgtc gcaagggcat gtttgaaact ccagaagaga agatagcaga aaactttctt 180  
 10 cagggttcggg aaatagctaa ggaagtcgag agtgacttgg tcattgctta tggggctgaa 240  
 atttactaca cgccagatgt tttggataag ctggaaaaca atcggattcc gaccctcaat 300  
 aatagtcggt atgccttgat agagtttagt atgaacactc cttatcgca tattcatagt 360  
 gccttgaata aaatattgat gttgggaatt actcccgta ttgccacat agagcgctat 420  
 gatgttcttg aaaataatga aaaacgcgtt cgagagctga tcgatatggg ctgttacacg 480  
 15 caaataaata gttcacatgt cctcaaactc aaactttttg gagaacctta taaattcatg 540  
 aaaaaaagag cgcagtattt cttggagcgt gatttgggtc atatcattgc aagtgatatg 600  
 cataatgtgg acggcagacc ccccatatg gcagaagcat atgacctgt tccccaaaa 660  
 tacggagaag cgaaggctca ggaacttttt atagacaatc ctgaaaaat tgaatggat 720  
 caactaattt ag 732

20

<210> 74  
 <211> 927  
 <212> DNA  
 <213> Streptococcus pneumoniae

25

<400> 74  
 atgtctacaa tcgataaaga aaaatttcag tttgtaaaac gtgacgattt tgcctctgaa 60  
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 aaatcaactg tagtcatgtt gggaatcttg gtagccatca ttttgataag tttcatctac 180  
 30 ccaatgtttt ctaagtttga tttcaatgat gtcagcaagg taaacgactt tagtggtcgt 240  
 tatatcaagc caaatgcgga gcattgggtc ggtactgaca gtaacggtaa atcgctcttt 300  
 gacggtgtct ggttcggagc tcgtaactcc atcctcattt ctgtgattgc gacagtgtt 360  
 aacttggtta tcggtgtttt tgtcgggtgtt atttggggtta tttcaaaatc agttgaccgt 420  
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 35 ttgacttact caatcggagc tggattcttg aaatcgtatt ttgccatgag cgtaacaaca 540  
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 40 cgtttgattt cggattattc aaaaaacgta acaaccaatg cttacttgtt ctggattcca 840  
 ttgacaacct ttgtcttggt atccttgtcc cttttcgtag ttggtcaaaa cttagcggat 900  
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45

<210> 75  
 <211> 234  
 <212> DNA  
 <213> Streptococcus pneumoniae

<400> 75  
 50 atgtataacc tattattaac ctttttatta gtattatctg ttgtgattgt gattgcaatt 60  
 ttcattgcaac caacaaaaa ccaatccagc aatgtatttg atgccagttc aggtgatttg 120  
 tttgaacgca gtaaagctcg cggttttgaa gctgtaatgc agcgtttgac agggatttta 180  
 gtctttttct ggctagccat tgccttagca ttgacggtat tatcaagtag ataa 234

55

<210> 76  
 <211> 1110  
 <212> DNA

<213> *Streptococcus pneumoniae*

&lt;400&gt; 76

5 atgttttcgta gaaataaatt attttttttg accacagaaa ttttactctt aaccatcatc 60  
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 attatgattc cttttttatt agggggcttt ctttattatt tgacaaaccc tattgttact 180  
 ttcttaataa agtctgttaa actcaatcgt ttgcttggtta ttttaattac cttgtgtact 240  
 ttggtctggg gaatggcat aggtgttggtc tatctcttac ctattttgat taatcagtta 300  
 10 tctagtttga ttatatctag tcaaactatt tatagtcgag tacaagactt aatcatagac 360  
 ttatctaatt atcctgctgt ccagaatttg gatgtagaag ctacaattca gcagttaaac 420  
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 gtcttgtcag ctcttatcag tactgttttg attttgatta tgactccagt ttttttggtt 540  
 ttttcttat tagatggaca taaattcttg cccatgcttg aaagaacgat tctaaagagg 600  
 gatcgcttgc atattgcagg cttattaaag aatttaaag cgacgattgc tcgctatatt 660  
 15 agtggagttt cgattgacgc aatcattata ggttggttggt cttatattgg ctatagtatt 720  
 attggtttta aatatgcttt agtttttgcc attttttctg gtgtagccaa ttttaattcct 780  
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 20 cttttgttgt caagcaatat ctatggtgta gttggaatga ttgtcgcagt gccaacctat 1020  
 tctatcttga aagaaatttc taagttctta tcccgtttgt atgaaaatca taaaataatg 1080  
 aaagaacgag aaagagaatt agctaagtaa 1110

&lt;210&gt; 77

25 &lt;211&gt; 1356

&lt;212&gt; DNA

<213> *Streptococcus pneumoniae*

&lt;400&gt; 77

30 atgtatcaag cactttatcg aaaatataga agtcaaaact tctcccagtt agttggtcaa 60  
 gaagtgtggt ctaagactct taaacaagcg gtggagcaag agaaaaataag tcacgccttat 120  
 cttttttctg gtcctcgtgg aacgggaaaa accagtgttg ctaaaatctt tgccaaggct 180  
 atgaactgtc ccaatcaagt ggggtggcgaa ccttgcaata actgctatat ttgtcaagca 240  
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 35 gatgaaattc gcgaaattcg tgataaatct acctatgcgc ctagccttgc tcgttataag 360  
 gtttatatca tagatgaggt tcacatgctg tctacagggg cttttaatgc cctcctaaag 420  
 acgctggaag aaccaacaca gaatgtagtc tttatttttg ccactactga attgcacaag 480  
 attcctgcta ctattctatc ccgtgtgcaa cgttttgagt ttaaatcaat taagacacag 540  
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 40 gctgtggaaa tcattgccag acgggcgga ggtggaatgc gggacgcctt gtctattttg 660  
 gatcaagccc tgagtttgac acagggaaat gagctgacga ctgctatctc tgaagaaatt 720  
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 45 aatactcatc atagtccagt cttgttagaa aatttggcac ttcctcaaaa aaatctgttt 960  
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 50 ggcaaaacag tctatcgtgt cgatcgcaat aaagtgaat ctatcttaca agaggccgctc 1260  
 gaaaatcctg atttaacacg tcaaaatcta attcgtttgc agaatgcatg gggagaggta 1320  
 attgaaagtc taggtgggac ggacaagctc tgctag 1356

&lt;210&gt; 78

55 &lt;211&gt; 1989

&lt;212&gt; DNA

<213> *Streptococcus pneumoniae*



<400> 78  
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 tatecttttg cgtggtgtgt tctcttggca gtcactctca cctatctctt ttactctcta 120  
 5 accttcaatc ctaagattgc ggaaatccgt ggaggaacaa ccattcaggc tacacttgga 180  
 tttggtatgt ttgtcgtcac ccttgcgtca gccattatcg ttctctatgc caatagtttt 240  
 gtcatagaaga aacgtttccaa ggaactagga atttatggca tgttgggctt ggagaagcgt 300  
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 10 aaattgaagg ttgagctggt tgctaccttc cagacgaaag ttgtcattac agtgcttggt 480  
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 15 acttatctct tgtttaatgc agggattacc gttttcctcc aaatcttaaa gaaaaataag 780  
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 gattttgggg tttcaggaca aaatggtgaa aaagaagatt tggacaaact cttgagccag 1020  
 20 tttgcaagtg acaatggtta taagattaaa gaaaaagaag tgtttcgtta cacttacttt 1080  
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 30 atcggtattt tctatccat tatctttatg gtcggaactg ttctggtcat ctactacaaa 1680  
 caaatttctg aaggctacga agacgtgaa cgctttatta tcttgcaaaa agtcggtttg 1740  
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 gtgattggtg tactggatgc gactatgatg ttgattgtga ccttgtctat ctgcgctatc 1920  
 35 ttcctcatcg cctatgtgct gattttcatg attacttcaa gaagttatcg caagattgtg 1980  
 caaatgtaa 1989

&lt;210&gt; 79

&lt;211&gt; 891

40 &lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

<400> 79  
 atgaaacaag atcaactaaa ggcttggcaa ccagctcagt ttgaccgttt tgtccgtatc 60  
 45 ttagaacaag accagctcaa tcacgcctat ctcttttcag gtttcttttg aagcttgga 120  
 atggcgcaat ttttagctaa gagcctcttt tgtacggata aagttggcgt cttaccatgt 180  
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 <213> Streptococcus pneumoniae

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 ggagaatacc ttctcctcgg agatgaccgc ttggtttcga gcgacagccg ccacgtaggt 540  
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20 <210> 81  
 <211> 987  
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25 <400> 81  
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45 <210> 82  
 <211> 1383  
 <212> DNA  
 <213> Streptococcus pneumoniae

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 15 gttgggtgctg gttcaactat tactaaagac gtgccagcag atgctattgc tattgggtcg 1320  
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<210> 83

20 <211> 936

<212> DNA

<213> Streptococcus pneumoniae

<400> 83

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 aatttcaaac ttgaaaacaa tcatgccttc cttgctgggt ccgtttcacg taagaaacaa 900  
 40 gtggtacctc aattaactga aagctttaat acgtaa 936

<210> 84

<211> 678

<212> DNA

45 <213> Streptococcus pneumoniae

<400> 84

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 50 agcgtattg cagggtagggt ggtggaagg cctatcagt ctgcggttaa aaatgttgag 180  
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 55 agcatcttag aagaagctgg aaagttttat gagattttgg tgggtggaagc aggacaaatg 480  
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gaaaaaaatc tggaagaacg tcaagttcta gtagataaga ttcaagctat caaggaggtg 660  
ctccatgtta gcaagtga 678

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<211> 486  
<212> DNA  
<213> Streptococcus pneumoniae

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20 <210> 86  
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<212> DNA  
<213> Streptococcus pneumoniae

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<210> 87  
<211> 1080  
50 <212> DNA  
<213> Streptococcus pneumoniae

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25 <210> 90  
 <211> 693  
 <212> DNA  
 <213> Streptococcus pneumoniae

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45 <210> 91  
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 <212> DNA  
 <213> Streptococcus pneumoniae

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&lt;210&gt; 94

&lt;211&gt; 978

25 &lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 94

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&lt;210&gt; 95

&lt;211&gt; 750

&lt;212&gt; DNA

50 &lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 95

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&lt;211&gt; 921

&lt;212&gt; DNA

15 <213> *Streptococcus pneumoniae*

&lt;400&gt; 97

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35 &lt;210&gt; 98

&lt;211&gt; 741

&lt;212&gt; DNA

<213> *Streptococcus pneumoniae*

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55 &lt;210&gt; 99

&lt;211&gt; 831

&lt;212&gt; DNA

<213> Streptococcus pneumoniae

<400> 99

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20 <211> 1623

<212> DNA

<213> Streptococcus pneumoniae

<400> 100

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55 <211> 1446

<212> DNA

<213> Streptococcus pneumoniae

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&lt;211&gt; 1176

&lt;212&gt; DNA

15 &lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 103

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&lt;210&gt; 104

40 &lt;211&gt; 696

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 104

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5

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15

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20

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&lt;400&gt; 108

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&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

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&lt;210&gt; 110

&lt;211&gt; 789

&lt;212&gt; DNA

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 110

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cgtgcgaatc atgataaaaa tttgcgtatt aagagtttag aagagcggtt gtcttacttt 180  
 gatgaaataa aagattcatt gagccagtct gtaattgattg ctccaggatac agctgagaga 240  
 gtgaaacagg cggcgcatga acgttcaaac aatatcattc atcaagcaga gcaagatgcg 300  
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 caacgtctca aatctacaat tgagagtcag ttggctattg ttgaatcttc agattgggaa 480  
 gatattctcc gtccaacagc tacttatctt caaacagtg atgaagcctt taaagaagtg 540  
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 aaagaattgt ctgaatttga agctcagatt aaacaggaag tggaagctcc aactcctgta 720  
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 cacttgattg gacaaagtca agtggctttc cgtgaatgga atcaaaaatg ggtcgattta 240  
 25 tctctcaact cttttgccga tattgaaaat aatctctttg aagcagaagg ttataacccat 300  
 tcatttcgtt ttctcaaggc cagtcaccaa attgaccaa ttgagagtca aattactttg 360  
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 aaaaatagtg gtcgtgttct tcatgctttg gatttatttg aggaacttca gcatagagtt 480  
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 35 atttttactc gagaaattgc tgctcagaaa gtagtggaat atctacttgc aactcttcca 960  
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 aacaagacct atttacttcc tgagacagct gcaagccatg ttcgtcgtat tcagacagaa 1080  
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 40 gatgagcaaa tttcagtttag tgagcgctg acacaaattg agaaagatga tattaatgca 1260  
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|    |                                |             |            |            |            |            |      |
|----|--------------------------------|-------------|------------|------------|------------|------------|------|
|    | ggctctctcaa                    | aaattgtcgt  | cggtgaggtc | ttgtcttgcg | aagatgtgcc | agagactcac | 180  |
|    | ctccatgttt                     | gtcagggttaa | cgttggcgaa | gaagagcgtc | agatcgtttg | tggtgcccca | 240  |
|    | aatgtgcgtg                     | ctgggatcaa  | ggcatggtg  | gtctctccag | gagctcgtat | cgctgataac | 300  |
|    | tacaaaatca                     | aaaaagga    | aatccgtggt | ttggagtcac | ttggaatgat | ctgttcactt | 360  |
| 5  | ggtgaattgg                     | gaatttctga  | ctcagttgtg | cctaaggaat | tcgcagatgg | catccaaatc | 420  |
|    | ttgcctgaag                     | atgccgtgcc  | aggtgaggaa | gtcttttctt | acctagactt | ggatgatgaa | 480  |
|    | atcatcgaac                     | tttccatcac  | accaaaccgt | gcagatgccc | tttctatgtg | tggagtggct | 540  |
|    | cacgaagtgg                     | cagccatcta  | tgacaaggca | gtcaacttta | aagaatttac | tctaacagaa | 600  |
|    | actaatgaag                     | ctgcggcaga  | tgccctttct | gtcagcattg | agacagacaa | ggcgccttac | 660  |
| 10 | tatgcagctc                     | gtatcttgga  | caatgtgacc | atcgacacaa | gtccacaatg | gttgcaaaac | 720  |
|    | cttctcatga                     | acgaaggaat  | ccgtcccatc | aataacgtag | tggacgtgac | caactacatc | 780  |
|    | ctgctctatt                     | ttggtcaacc  | aatgcatgcc | tttgacttgg | ataactttga | agggactgac | 840  |
|    | atccgtgtgc                     | gtgaagcgcg  | tgctgggtga | aaattggtga | ccttggacgg | tgaagaacgt | 900  |
|    | gacttggacg                     | tgaatgacct  | agtcatact  | gtcgcagaca | agccagtagc | ccttgcaggt | 960  |
| 15 | gtcatgggtg                     | gtcaagcaac  | agaaatctct | gaaaaatcta | gtcgtgttgt | ccttgaagct | 1020 |
|    | gctgttttca                     | atggcaaatc  | tatccgtaag | acaagtggtc | gcctgaacct | tcgttctgag | 1080 |
|    | tcatcttctc                     | gctttgaaaa  | aggaattaat | gtggcaacag | ttaatgaagc | ccttgatgcg | 1140 |
|    | gcagctagcc                     | tgattgcgga  | acttgcaggt | gcgacgggtg | gtaagggcat | cgtttcagcg | 1200 |
|    | ggtgagcttg                     | atacttcaga  | tgtagaagtt | tcttcaaccc | ttgctgatgt | taaccgtgtc | 1260 |
| 20 | ctcggaaactg                    | agctgtctta  | tgctgatgta | gaagacgtct | tcgctcgtct | tggcttttgt | 1320 |
|    | ctttctgtaa                     | atgcagacag  | ctttacagtc | agagtccac  | gtcgtcgttg | ggatatcaca | 1380 |
|    | atcgaagctg                     | acctctttga  | agaaattgct | cgtatctatg | gttatgaccg | cttgccaact | 1440 |
|    | agtctaccaa                     | aagacgatgg  | tacagcaggt | gaattgacag | ccacacaaaa | actccgccgt | 1500 |
|    | caagttcgtg                     | ctattgctga  | aggagcaggt | ttgacagaaa | tcatcaccta | tactctaaca | 1560 |
| 25 | actcctgaaa                     | aagcagttga  | gtttacggct | caaccaagta | accttacgga | actcatgttg | 1620 |
|    | ccaatgactg                     | tggatcgctc  | agtcctccgt | caaaatatga | tttcaggtat | ccttgatacc | 1680 |
|    | gttgcctaca                     | acgtggctcg  | taagaataaa | aacttggccc | tttacgagat | tggaaaagtc | 1740 |
|    | tttgaacaaa                     | caggtaatcc  | aaaagaagaa | cttccaaatg | aatcaacag  | ttttgccttt | 1800 |
|    | gccttgacag                     | gcttgggtgc  | tgaaaaagat | ttccaaacag | cagcagttcc | agttgatttc | 1860 |
| 30 | ttctatgcta                     | agggaatcct  | tgaagcccta | tttactcgtt | tgggactcca | agtaacctat | 1920 |
|    | acagcaacat                     | ctgaaatcgc  | tagccttcat | ccaggtcgtg | cagccgtgat | ttcactcggg | 1980 |
|    | gaccaagttc                     | ttggtttcct  | tggccaagtg | catccagtca | ctgccaaggc | ttacgatatt | 2040 |
|    | ccagaaacgt                     | atgtggctga  | gcttaacctt | tcagctatcg | aagctgcgct | tcagccagcg | 2100 |
|    | actccatttg                     | tagaaatcac  | caaattcccg | gcagtcagcc | gtgacgttgc | ccttctcttc | 2160 |
| 35 | aaggcagaag                     | tgactcatca  | agaagttgta | gatgctatcc | aagctgccgg | cgtgaaacgt | 2220 |
|    | ttgacagata                     | tcaaactctt  | tgacgtcttc | tcaggtgaga | aattgggact | tggatgaag  | 2280 |
|    | tcaatggctt                     | atagcttgac  | cttccaaaat | ccagaagata | gcttaacgga | cgaagaagtc | 2340 |
|    | gcacgtata                      | tggaaaaaat  | ccaagcatcg | ctcgaagaaa | aagtcaatgc | agaagtgcgt | 2400 |
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|    | <211> 543                      |             |            |            |            |            |      |
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|    | <213> Streptococcus pneumoniae |             |            |            |            |            |      |
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|    | aaaaaactag                     | gtgctcaatt  | aactaaagat | tatgcaggaa | aaaatccaat | cttagttggg | 120  |
|    | attttaaaag                     | gatctattcc  | ttttatggct | gaattggtca | aacatattga | tacacatatt | 180  |
| 50 | gaaatggact                     | tcattgatgt  | ttctagctac | catggtggaa | cagcaagtag | tgggtgtatc | 240  |
|    | aatattaaac                     | aagatgtgac  | tcaagatata | aaaggaagac | atgttctatt | tgtagaagat | 300  |
|    | atcattgata                     | caggtcaaac  | tttgaagaat | ttgcgagata | tgtttaaagc | aagagaagca | 360  |
|    | gcttctgtta                     | aaattgcaac  | cttgttggat | aaaccagaag | gacgtgttgt | agaaattgag | 420  |
|    | gcagactata                     | cctgctttac  | tatcccaaat | gagttttag  | taggttatgg | tttagactac | 480  |
| 55 | aaagaaaatt                     | atcgtaattc  | tccttatatt | ggagtattga | aagaggaagt | gtattcaaat | 540  |
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5

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Leu Ile His Thr Ile Glu Lys Phe Val Leu Glu Pro Ser Ile Glu Lys  
 35 40 45

15

Ile Val Val Gly Val His Gly Asp Trp Val Leu His Ala Glu Asp Leu  
 50 55 60

Val Asp Lys Tyr Leu Pro Leu His Lys Glu Arg Ile Ile Ile Thr Lys  
 65 70 75 80

20

Gly Gly Ala Asp Arg Asn Thr Ser Ile Glu Asn Ile Ile Glu Ala Ile  
 85 90 95

25

Asp Ala Tyr Arg Pro Leu Thr Pro Glu Asp Ile Val Val Thr His Asp  
 100 105 110

Ser Val Arg Pro Phe Ile Thr Leu Arg Met Ile Gln Asp Ser Ile Lys  
 115 120 125

30

Leu Ala Gln Asn His Asp Ala Val Asp Thr Val Val Glu Ala Val Asp  
 130 135 140

Thr Ile Val Glu Ser Thr Asn Gly Gln Phe Ile Thr Gly Ile Pro Asn  
 145 150 155 160

35

Arg Ala His Leu Tyr Gln Gly Gln Thr Pro Gln Thr Phe Arg Cys Lys  
 165 170 175

40

Asp Phe Met Asp Leu Tyr Gly Ser Leu Ser Asp Glu Glu Lys Glu Ile  
 180 185 190

Leu Thr Asp Ala Cys Lys Ile Phe Val Ile Lys Gly Lys Asp Val Ala  
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50

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 <212> PRT  
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55

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 Asn Ala Ser Leu Leu Asp Arg Val His Val Glu Tyr Tyr Gly Val Glu  
 35 40 45  
 10 Thr Pro Leu Asn Gln Ile Ala Ser Ile Thr Ile Pro Glu Ala Arg Val  
 50 55 60  
 Leu Leu Val Thr Pro Phe Asp Lys Ser Ser Leu Lys Asp Ile Glu Arg  
 15 65 70 75 80  
 Ala Leu Asn Ala Ser Asp Leu Gly Ile Thr Pro Ala Asn Asp Gly Ser  
 85 90 95  
 20 Val Ile Arg Leu Val Ile Pro Ala Leu Thr Glu Glu Thr Arg Arg Asp  
 100 105 110  
 Leu Ala Lys Glu Val Lys Lys Val Gly Glu Asn Ala Lys Val Ala Val  
 115 120 125  
 25 Arg Asn Ile Arg Arg Asp Ala Met Asp Glu Ala Lys Lys Gln Glu Lys  
 130 135 140  
 Ala Gln Glu Ile Thr Glu Asp Glu Leu Lys Thr Leu Glu Lys Asp Ile  
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 Gln Lys Val Thr Asp Asp Ala Val Lys His Ile Asp Asp Met Thr Ala  
 165 170 175  
 35 Asn Lys Glu Lys Glu Leu Leu Glu Val  
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 40 <211> 450  
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 50 Val Leu Ser Gln His Glu Thr Glu Ala Pro Lys Val Phe Val Gly Arg  
 35 40 45  
 Asp Thr Arg Ile Ser Gly Glu Met Leu Glu Ser Ala Leu Val Ala Gly  
 55 50 55 60  
 Leu Leu Ser Val Gly Ile His Val Tyr Lys Leu Gly Val Leu Ala Thr

51 .

370                      375                      380  
 Lys Ala Met Glu Val Pro Ala Ile Lys Ala Ile Ile Glu Lys Met Glu  
 385                      390                      395                      400  
 5      Glu Glu Met Ala Gly Asn Gly Arg Ile Leu Val Arg Pro Ser Gly Thr  
                                  405                      410                      415  
 10     Glu Pro Leu Leu Arg Val Met Ala Glu Ala Pro Thr Thr Glu Glu Val  
                                  420                      425                      430  
     Asp Tyr Tyr Val Asp Thr Ile Thr Asp Val Val Arg Ala Glu Ile Gly  
                                  435                      440                      445  
 15     Ile Asp  
                                  450  
  
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                                  20                      25                      30  
 30     Asn Gly Arg Glu Ala Leu Glu Gln Phe Glu Ala Glu Gln Pro Asp Ile  
                                  35                      40                      45  
 35     Ile Ile Leu Asp Leu Met Leu Pro Glu Ile Asp Gly Leu Glu Val Ala  
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     Lys Thr Ile Arg Lys Thr Ser Ser Val Pro Ile Leu Met Leu Ser Ala  
         65                      70                      75                      80  
 40     Lys Asp Ser Glu Phe Asp Lys Val Ile Gly Leu Glu Leu Gly Ala Asp  
                                  85                      90                      95  
     Asp Tyr Val Thr Lys Pro Phe Ser Asn Arg Glu Leu Gln Ala Arg Val  
                                  100                      105                      110  
 45     Lys Ala Leu Leu Arg Arg Ser Gln Pro Met Pro Val Asp Gly Gln Glu  
                                  115                      120                      125  
 50     Ala Asp Ser Lys Pro Gln Pro Ile Gln Ile Gly Asp Leu Glu Ile Val  
         130                      135                      140  
     Pro Asp Ala Tyr Val Ala Lys Lys Tyr Gly Glu Glu Leu Asp Leu Thr  
         145                      150                      155                      160  
 55     His Arg Glu Phe Glu Leu Leu Tyr His Leu Ala Ser His Thr Gly Gln  
                                  165                      170                      175

Val Ile Thr Arg Glu His Leu Leu Glu Thr Val Trp Gly Tyr Asp Tyr  
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 5 Phe Gly Asp Val Arg Thr Val Asp Val Thr Val Arg Arg Leu Arg Glu  
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 25 Leu Glu Thr Gly Glu Val Tyr Cys Gln Arg Cys Phe Arg Leu Arg His  
 35 40 45  
 Tyr Asn Glu Ile Thr Asp Val Gln Leu Thr Asn Asp Asp Phe Leu Lys  
 30 50 55 60  
 Leu Leu His Glu Val Gly Asp Ser Asp Ala Leu Val Val Asn Val Ile  
 65 70 75 80  
 35 Asp Ile Phe Asp Phe Asn Gly Ser Val Ile Pro Gly Leu Pro Arg Phe  
 85 90 95  
 Val Ser Gly Asn Asp Val Leu Leu Val Gly Asn Lys Lys Asp Ile Leu  
 100 105 110  
 40 Pro Lys Ser Val Lys Ser Gly Lys Ile Ser Gln Trp Leu Met Lys Arg  
 115 120 125  
 Ala His Glu Glu Gly Leu Arg Pro Val Asp Val Val Leu Thr Ser Ala  
 45 130 135 140  
 Gln Asn Lys His Ala Ile Lys Glu Val Ile Asp Lys Ile Glu His Tyr  
 145 150 155 160  
 50 Arg Lys Gly Arg Asp Val Tyr Val Val Gly Val Thr Asn Val Gly Lys  
 165 170 175  
 Ser Thr Leu Ile Asn Ala Ile Ile Gln Glu Ile Thr Gly Asp Gln Asn  
 180 185 190  
 55 Val Ile Thr Thr Ser Arg Phe Pro Gly Thr Thr Leu Asp Lys Ile Glu  
 195 200 205

Ile Pro Leu Asp Asp Gly Ser Tyr Ile Tyr Asp Thr Pro Gly Ile Ile  
 210 215 220  
 5 His Arg His Gln Met Ala His Tyr Leu Thr Ala Lys Asn Leu Lys Tyr  
 225 230 235 240  
 Val Ser Pro Lys Lys Glu Ile Lys Pro Lys Thr Tyr Gln Leu Asn Pro  
 245 250 255  
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 260 265 270  
 Gly Glu Lys Gln Gly Phe Thr Ala Phe Phe Asp Asn Glu Leu Lys Leu  
 15 275 280 285  
 His Arg Ser Lys Leu Glu Gly Ala Ser Ala Phe Tyr Asp Lys His Leu  
 290 295 300  
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 305 310 315 320  
 Arg Leu Val Gln His Val Phe Thr Ile Lys Asp Lys Thr Asp Leu Val  
 325 330 335  
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 35 40 45  
 50 Val Phe Ala Gly Leu Glu Arg Ile Val Asn Tyr Leu Glu Asp Leu Arg  
 50 55 60  
 Phe Ser Asp Ser Asp Ile Ala Tyr Leu Glu Ser Leu Gly Tyr His Gly  
 55 65 70 75 80  
 Ala Phe Leu Asp Tyr Leu Arg Asn Phe Lys Leu Glu Leu Thr Val Arg



|    | 85  | 90  | 95  |
|----|---|-----|-----|
|    | Ser Ala Gln Glu Gly Asp Leu Val Phe Ala Asn Glu Pro Ile Val Gln |     |     |
|    | 100   | 105 | 110 |
| 5  | Val Glu Gly Pro Leu Ala Gln Cys Gln Leu Val Glu Thr Ala Leu Leu |     |     |
|    | 115   | 120 | 125 |
|    | Asn Ile Val Asn Tyr Gln Thr Leu Val Ala Thr Lys Ala Ala Arg Ile |     |     |
| 10 | 130   | 135 | 140 |
|    | Arg Ser Val Ile Glu Asp Glu Pro Leu Met Glu Phe Gly Thr Arg Arg |     |     |
|    | 145   | 150 | 155 |
| 15 | Ala Gln Glu Thr Asp Ala Ala Ile Trp Gly Thr Arg Ala Ala Val Ile |     |     |
|    | 165   | 170 | 175 |
|    | Gly Gly Ala Asn Gly Thr Ser Asn Val Arg Ala Gly Lys Leu Phe Asp |     |     |
|    | 180   | 185 | 190 |
| 20 | Ile Pro Val Leu Gly Thr His Ala His Ala Leu Val Gln Val Tyr Gly |     |     |
|    | 195   | 200 | 205 |
|    | Asn Asp Tyr Glu Ala Phe Lys Ala Tyr Ala Ala Thr His Lys Asn Cys |     |     |
| 25 | 210   | 215 | 220 |
|    | Val Phe Leu Val Asp Thr Tyr Asp Thr Leu Arg Ile Gly Val Pro Ala |     |     |
|    | 225   | 230 | 235 |
| 30 | Ala Ile Gln Val Ala Arg Glu Leu Gly Asp Gln Ile Asn Phe Met Gly |     |     |
|    | 245   | 250 | 255 |
|    | Val Arg Ile Asp Ser Gly Asp Ile Ala Tyr Ile Ser Lys Lys Val Arg |     |     |
|    | 260   | 265 | 270 |
| 35 | Gln Gln Leu Asp Glu Ala Gly Phe Thr Glu Ala Lys Ile Tyr Ala Ser |     |     |
|    | 275   | 280 | 285 |
|    | Asn Asp Leu Asp Glu Asn Thr Ile Leu Asn Leu Lys Met Gln Lys Ala |     |     |
| 40 | 290   | 295 | 300 |
|    | Lys Ile Asp Val Trp Gly Val Gly Thr Gln Leu Ile Thr Ala Tyr Asp |     |     |
|    | 305   | 310 | 315 |
| 45 | Gln Pro Ala Leu Gly Ala Val Tyr Lys Ile Val Ala Ile Glu Asp Glu |     |     |
|    | 325   | 330 | 335 |
|    | Thr Gly Gln Met Arg Asn Thr Ile Lys Leu Ser Asn Asn Ala Glu Lys |     |     |
|    | 340   | 345 | 350 |
| 50 | Val Ser Thr Pro Gly Lys Lys Gln Val Trp Arg Ile Thr Ser Arg Glu |     |     |
|    | 355   | 360 | 365 |
|    | Lys Gly Lys Ser Glu Gly Asp Tyr Ile Thr Tyr Asp Gly Val Asp Ile |     |     |
| 55 | 370   | 375 | 380 |
|    | Ser Asp Met Thr Glu Ile Lys Met Phe His Pro Thr Tyr Thr Tyr Ile |     |     |

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 Lys Lys Thr Val Arg Asn Phe Asp Ala Val Pro Leu Leu Val Asp Ile  
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 5 Phe Lys Glu Gly Ile Leu Val Tyr Asn Leu Pro Ser Leu Thr Asp Ile  
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 10 Gln Asp Tyr Ala Arg Lys Glu Phe Asp Lys Leu Trp Asp Glu Tyr Lys  
                                  435                      440                      445  
 Arg Val Leu Asn Pro Gln His Tyr Pro Val Asp Leu Ala Arg Asp Val  
                                  450                      455                      460  
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       1                      5                      10                      15  
 30 Gln Val Gln Glu Asn Leu Lys Phe Val Asp Phe Val Thr Ile Leu Val  
                                  20                      25                      30  
 35 Asp Ala Arg Leu Pro Leu Ser Ser Gln Asn Pro Met Leu Thr Lys Ile  
                                  35                      40                      45  
 Val Gly Asp Lys Pro Lys Leu Ile Leu Asn Lys Ala Asp Leu Ala  
                                  50                      55                      60  
 40 Asp Pro Ala Met Thr Lys Glu Trp Arg Gln Tyr Phe Glu Ser Gln Gly  
                                  65                      70                      75                      80  
 Ile Gln Thr Leu Ala Ile Asn Ser Lys Glu Gln Val Thr Val Lys Val  
                                  85                      90                      95  
 45 Val Thr Asp Ala Ala Lys Lys Leu Met Ala Asp Lys Ile Ala Arg Gln  
                                  100                      105                      110  
 50 Lys Glu Arg Gly Ile Gln Ile Glu Thr Leu Arg Thr Met Ile Ile Gly  
                                  115                      120                      125  
 Ile Pro Asn Ala Gly Lys Ser Thr Leu Met Asn Arg Leu Ala Gly Lys  
                                  130                      135                      140  
 55 Lys Ile Ala Val Val Gly Asn Lys Pro Gly Val Thr Lys Gly Gln Gln  
                                  145                      150                      155                      160

Trp Leu Lys Thr Asn Lys Asp Leu Glu Ile Leu Asp Thr Pro Gly Ile  
 165 170 175  
 5 Leu Trp Pro Lys Phe Glu Asp Glu Thr Val Ala Leu Lys Leu Ala Leu  
 180 185 190  
 Thr Gly Ala Ile Lys Asp Gln Leu Leu Pro Met Asp Glu Val Thr Ile  
 195 200 205  
 10 Phe Gly Ile Asn Tyr Phe Lys Glu His Tyr Pro Glu Lys Leu Ala Glu  
 210 215 220  
 Arg Phe Lys Gln Met Lys Ile Glu Glu Glu Pro Ser Val Ile Ile Met  
 225 230 235 240  
 15 Asp Met Thr Arg Ala Leu Gly Phe Arg Asp Asp Tyr Asp Arg Phe Tyr  
 245 250 255  
 20 Ser Leu Phe Val Lys Glu Val Arg Asp Gly Lys Leu Gly Asn Tyr Thr  
 260 265 270  
 Leu Asp Thr Leu Glu Asp Leu Asp Gly Asn Asp  
 275 280  
 25  
 <210> 121  
 <211> 156  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 30  
 <400> 121  
 Met Ile Asn Asn Val Val Leu Val Gly Arg Met Thr Arg Asp Ala Glu  
 1 5 10 15  
 35 Leu Arg Tyr Thr Pro Ser Asn Val Ala Val Ala Thr Phe Thr Leu Ala  
 20 25 30  
 Val Asn Arg Thr Phe Lys Ser Gln Asn Gly Glu Arg Glu Ala Asp Phe  
 35 40 45  
 40 Ile Asn Val Val Met Trp Arg Gln Gln Ala Glu Asn Leu Ala Asn Trp  
 50 55 60  
 Ala Lys Lys Gly Ser Leu Ile Gly Val Thr Gly Arg Ile Gln Thr Arg  
 45 65 70 75 80  
 Ser Tyr Asp Asn Gln Gln Gly Gln Arg Val Tyr Val Thr Glu Val Val  
 85 90 95  
 50 Ala Glu Asn Phe Gln Met Leu Glu Ser Arg Ser Val Arg Glu Gly His  
 100 105 110  
 Thr Gly Gly Ala Tyr Ser Ala Pro Thr Ala Asn Tyr Ser Ala Pro Thr  
 115 120 125  
 55 Asn Ser Val Pro Asp Phe Ser Arg Asn Glu Asn Pro Phe Gly Ala Thr  
 130 135 140

Asn Pro Leu Asp Ile Ser Asp Asp Asp Leu Pro Phe  
 145 150 155

5  
 <210> 122  
 <211> 324  
 <212> PRT  
 <213> Streptococcus pneumoniae

10  
 <400> 122  
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 1 5 10 15

15  
 Gln Gly Gly Met Ala Trp Val Ala Asp Gly Asp Leu Ala Gly Ala Val  
 20 25 30

Ser Lys Ala Gly Gly Leu Gly Ile Ile Gly Gly Gly Asn Ala Pro Lys  
 35 40 45

20  
 Glu Val Val Lys Ala Asn Ile Asp Lys Ile Lys Ser Leu Thr Asp Lys  
 50 55 60

25  
 Pro Phe Gly Val Asn Ile Met Leu Leu Ser Pro Phe Val Glu Asp Ile  
 65 70 75 80

Val Asp Leu Val Ile Glu Glu Gly Val Lys Val Val Thr Thr Gly Ala  
 85 90 95

30  
 Gly Asn Pro Ser Lys Tyr Met Glu Arg Phe His Glu Ala Gly Ile Ile  
 100 105 110

Val Ile Pro Val Val Pro Ser Val Ala Leu Ala Lys Arg Met Glu Lys  
 115 120 125

35  
 Ile Gly Ala Asp Ala Val Ile Ala Glu Gly Met Glu Ala Gly Gly His  
 130 135 140

40  
 Ile Gly Lys Leu Thr Thr Met Thr Leu Val Arg Gln Val Ala Thr Ala  
 145 150 155 160

Ile Ser Ile Pro Val Ile Ala Ala Gly Gly Ile Ala Asp Gly Glu Gly  
 165 170 175

45  
 Ala Ala Ala Gly Phe Met Leu Gly Ala Glu Ala Val Gln Val Gly Thr  
 180 185 190

Arg Phe Val Val Ala Lys Glu Ser Asn Ala His Pro Asn Tyr Lys Glu  
 195 200 205

50  
 Lys Ile Leu Lys Ala Arg Asp Ile Asp Thr Thr Ile Ser Ala Gln His  
 210 215 220

55  
 Phe Gly His Ala Val Arg Ala Ile Lys Asn Gln Leu Thr Arg Asp Phe  
 225 230 235 240

Glu Leu Ala Glu Lys Asp Ala Phe Lys Gln Glu Asp Pro Asp Leu Glu

245                      250                      255  
 Ile Phe Glu Gln Met Gly Ala Gly Ala Leu Ala Lys Ala Val Val His  
                          260                      265                      270  
 5 Gly Asp Val Glu Gly Gly Ser Val Met Ala Gly Gln Ile Ala Gly Leu  
                          275                      280                      285  
 Val Ser Lys Glu Glu Thr Ala Glu Glu Ile Leu Lys Asp Leu Tyr Tyr  
 10                      290                      295                      300  
 Gly Ala Ala Lys Lys Ile Gln Glu Glu Ala Ser Arg Trp Thr Gly Val  
 305                      310                      315                      320  
 15 Val Arg Asn Asp  
  
 <210> 123  
 20 <211> 140  
     <212> PRT  
     <213> Streptococcus pneumoniae  
  
 <400> 123  
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     1                      5                      10                      15  
 Met Leu Leu Val Asp Arg Val Leu Glu Val Ser Glu Asp Thr Ile Val  
                          20                      25                      30  
 30 Ala Ile Lys Asn Val Thr Ile Asn Glu Pro Phe Phe Asn Gly His Phe  
                          35                      40                      45  
 Pro Gln Tyr Pro Val Met Pro Gly Val Leu Ile Met Glu Ala Leu Ala  
 35                      50                      55                      60  
 Gln Thr Ala Gly Val Leu Glu Leu Ser Lys Pro Glu Asn Lys Gly Lys  
     65                      70                      75                      80  
 40 Leu Val Phe Tyr Ala Gly Met Asp Lys Val Lys Phe Lys Lys Gln Val  
                          85                      90                      95  
 Val Pro Gly Asp Gln Leu Val Met Thr Ala Thr Phe Val Lys Arg Arg  
                          100                      105                      110  
 45 Gly Thr Ile Ala Val Val Glu Ala Lys Ala Glu Val Asp Gly Lys Leu  
                          115                      120                      125  
 Ala Ala Ser Gly Thr Leu Thr Phe Ala Ile Gly Asn  
 50                      130                      135                      140  
  
 <210> 124  
 <211> 340  
 55 <212> PRT  
     <213> Streptococcus pneumoniae

<400> 124  
Met Ile Asn Gln Ile Tyr Gln Leu Thr Lys Pro Lys Phe Ile Asn Val  
1 5 10 15  
5 Lys Tyr Gln Glu Glu Ala Ile Asp Gln Glu Asn His Ile Leu Ile Arg  
20 25 30  
Pro Asn Tyr Met Ala Val Cys His Ala Asp Gln Arg Tyr Tyr Gln Gly  
35 40 45  
10 Lys Arg Asp Pro Lys Ile Leu Asn Lys Lys Leu Pro Met Ala Met Ile  
50 55 60  
15 His Glu Ser Cys Gly Ile Val Ile Ser Asp Pro Ser Gly Thr Tyr Glu  
65 70 75 80  
Val Gly Gln Lys Val Val Met Ile Pro Asn Gln Ser Pro Met Gln Ser  
85 90 95  
20 Asp Glu Glu Phe Tyr Glu Asn Tyr Met Thr Gly Thr His Phe Leu Ser  
100 105 110  
Ser Gly Phe Asp Gly Phe Met Arg Glu Phe Val Ser Leu Pro Lys Asp  
115 120 125  
25 Arg Val Val Ala Tyr Asp Ala Ile Glu Asp Thr Val Ala Ala Ile Thr  
130 135 140  
30 Glu Phe Val Ser Val Gly Met His Ala Met Asn Arg Leu Leu Thr Leu  
145 150 155 160  
Ala His Ser Lys Arg Glu Arg Ile Pro Val Ile Gly Asp Gly Ser Leu  
165 170 175  
35 Ala Phe Val Val Ala Asn Ile Ile Asn Tyr Thr Leu Pro Glu Ala Glu  
180 185 190  
Ile Val Val Ile Gly Arg His Trp Glu Lys Leu Glu Leu Phe Ser Phe  
195 200 205  
40 Ala Lys Glu Cys Tyr Ile Thr Asp Asn Ile Pro Glu Glu Leu Ala Phe  
210 215 220  
45 Asp His Ala Phe Glu Cys Cys Gly Gly Asp Gly Thr Gly Pro Ala Ile  
225 230 235 240  
Asn Asp Leu Ile Arg Tyr Ile Arg Pro Gln Gly Thr Ile Leu Met Met  
245 250 255  
50 Gly Val Ser Glu Tyr Lys Val Asn Leu Asn Thr Arg Asp Ala Leu Glu  
260 265 270  
Lys Gly Leu Leu Leu Val Gly Ser Ser Arg Ser Gly Arg Ile Asp Phe  
275 280 285  
55 Glu Asn Ala Ile Gln Met Met Lys Val Lys Lys Phe Ala Asn Arg Leu  
290 295 300

Lys Asn Ile Leu Tyr Leu Glu Glu Pro Val Arg Glu Ile Lys Asp Ile  
 305 310 315 320  
 5 His Arg Val Phe Ala Thr Asp Leu Asn Thr Ala Phe Lys Thr Val Phe  
 325 330 335  
 Lys Trp Glu Val  
 340  
 10  
 <210> 125  
 <211> 447  
 <212> PRT  
 15 <213> Streptococcus pneumoniae  
 <400> 125  
 Met Asn Leu Lys Thr Thr Leu Gly Leu Leu Ala Gly Arg Ser Ser His  
 1 5 10 15  
 20 Phe Val Leu Ser Arg Leu Gly Arg Gly Ser Thr Leu Pro Gly Lys Val  
 20 25 30  
 25 Ala Leu Gln Phe Asp Lys Asp Ile Leu Gln Asn Leu Ala Lys Asn Tyr  
 35 40 45  
 Glu Ile Val Val Val Thr Gly Thr Asn Gly Lys Thr Leu Thr Thr Ala  
 50 55 60  
 30 Leu Thr Val Gly Ile Leu Lys Glu Val Tyr Gly Gln Val Leu Thr Asn  
 65 70 75 80  
 Pro Ser Gly Ala Asn Met Ile Thr Gly Ile Ala Thr Thr Phe Leu Thr  
 85 90 95  
 35 Ala Lys Ser Ser Lys Thr Gly Lys Asn Ile Ala Val Leu Glu Ile Asp  
 100 105 110  
 40 Glu Ala Ser Leu Ser Arg Ile Cys Asp Tyr Ile Gln Pro Ser Leu Phe  
 115 120 125  
 Val Ile Thr Asn Ile Phe Arg Asp Gln Met Asp Arg Phe Gly Glu Ile  
 130 135 140  
 45 Tyr Thr Thr Tyr Asn Met Ile Leu Asp Ala Ile Arg Lys Val Pro Thr  
 145 150 155 160  
 Ala Thr Val Leu Leu Asn Gly Asp Ser Pro Leu Phe Tyr Lys Pro Thr  
 165 170 175  
 50 Ile Pro Asn Pro Ile Glu Tyr Phe Gly Phe Asp Leu Glu Lys Gly Pro  
 180 185 190  
 55 Ala Gln Leu Ala His Tyr Asn Thr Glu Gly Ile Leu Cys Pro Asp Cys  
 195 200 205  
 Gln Gly Ile Leu Lys Tyr Glu His Asn Thr Tyr Ala Asn Leu Gly Ala

210 215 220  
 Tyr Ile Cys Glu Gly Cys Gly Cys Lys Arg Pro Asp Leu Asp Tyr Arg  
 225 230 235 240  
 5 Leu Thr Lys Leu Val Glu Leu Thr Asn Asn Arg Ser Arg Phe Val Ile  
 245 250 255  
 10 Asp Gly Gln Glu Tyr Gly Ile Gln Ile Gly Gly Leu Tyr Asn Ile Tyr  
 260 265 270  
 Asn Ala Leu Ala Ala Val Ala Ile Ala Arg Phe Leu Gly Ala Asp Ser  
 275 280 285  
 15 Gln Leu Ile Lys Gln Gly Phe Asp Lys Ser Arg Ala Val Phe Gly Arg  
 290 295 300  
 Gln Glu Thr Phe His Ile Gly Asp Lys Glu Cys Thr Leu Val Leu Ile  
 305 310 315 320  
 20 Lys Asn Pro Val Gly Ala Thr Gln Ala Ile Glu Met Ile Lys Leu Ala  
 325 330 335  
 25 Pro Tyr Pro Phe Ser Leu Ser Val Leu Leu Asn Ala Asn Tyr Ala Asp  
 340 345 350  
 Gly Ile Asp Thr Ser Trp Ile Trp Asp Ala Asp Phe Glu Gln Ile Thr  
 355 360 365  
 30 Asp Met Asp Ile Pro Glu Ile Asn Ala Gly Gly Val Arg His Ser Glu  
 370 375 380  
 Ile Ala Arg Arg Leu Arg Val Thr Gly Tyr Pro Ala Glu Lys Ile Thr  
 385 390 395 400  
 35 Glu Thr Ser Asn Leu Glu Gln Val Leu Lys Thr Ile Glu Asn Gln Asp  
 405 410 415  
 40 Cys Lys His Ala Tyr Ile Leu Ala Thr Tyr Thr Ala Met Leu Glu Phe  
 420 425 430  
 Arg Glu Leu Leu Ala Ser Arg Gln Ile Val Arg Lys Glu Met Asn  
 435 440 445  
 45  
 <210> 126  
 <211> 260  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 50  
 <400> 126  
 Met Val Tyr Thr Ser Leu Ser Ser Lys Asp Gly Asn Tyr Pro Tyr Gln  
 1 5 10 15  
 55 Leu Asn Ile Ala His Leu Tyr Gly Asn Leu Met Asn Thr Tyr Gly Asp  
 20 25 30



Asn Gly Asn Ile Leu Met Leu Lys Tyr Val Ala Glu Lys Leu Gly Ala  
 35 40 45  
 5 His Val Thr Val Asp Ile Val Ser Leu His Asp Asp Phe Asp Glu Asn  
 50 55 60  
 His Tyr Asp Ile Ala Phe Phe Gly Gly Gly Gln Asp Phe Glu Gln Ser  
 65 70 75 80  
 10 Ile Ile Ala Asp Asp Leu Pro Ala Lys Lys Glu Ser Ile Asp Asn Tyr  
 85 90 95  
 Ile Gln Asn Asp Gly Val Val Leu Ala Ile Cys Gly Gly Phe Gln Leu  
 100 105 110  
 15 Leu Gly Gln Tyr Tyr Val Glu Ala Ser Gly Lys Arg Ile Glu Gly Leu  
 115 120 125  
 20 Gly Val Met Gly His Tyr Thr Leu Asn Gln Thr Asn Asn Arg Phe Ile  
 130 135 140  
 Gly Asp Ile Lys Ile His Asn Glu Asp Phe Asp Glu Thr Tyr Tyr Gly  
 145 150 155 160  
 25 Phe Glu Asn His Gln Gly Arg Thr Phe Leu Ser Asp Asp Gln Lys Pro  
 165 170 175  
 Leu Gly Gln Val Val Tyr Gly Asn Gly Asn Asn Glu Glu Lys Val Gly  
 180 185 190  
 30 Glu Gly Val His Tyr Lys Asn Val Phe Gly Ser Tyr Phe His Gly Pro  
 195 200 205  
 35 Ile Leu Ser Arg Asn Ala Asn Leu Ala Tyr Arg Leu Val Thr Thr Ala  
 210 215 220  
 Leu Lys Lys Lys Tyr Gly Gln Asp Ile Gln Leu Pro Ala Tyr Glu Asp  
 225 230 235 240  
 40 Ile Leu Ser Gln Glu Ile Ala Glu Glu Tyr Ser Asp Val Lys Ser Lys  
 245 250 255  
 Ala Asp Phe Ser  
 260  
 45  
 <210> 127  
 <211> 223  
 <212> PRT  
 50 <213> Streptococcus pneumoniae  
 <400> 127  
 Met Asn Val Lys Glu Asn Thr Glu Leu Val Phe Arg Glu Val Ala Glu  
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 20 25 30

Val Thr Lys Tyr Val Asp Val Pro Thr Ala Glu Ala Leu Leu Pro Leu  
                   35                                  40                                  45

5 Gly Val His His Ile Gly Glu Asn Arg Val Asp Lys Phe Leu Glu Lys  
                   50                                  55                                  60

Tyr Glu Ala Leu Lys Asp Arg Asp Val Thr Trp His Leu Ile Gly Thr  
                   65                                  70                                  75                                  80

10 Leu Gln Arg Arg Lys Val Lys Asp Val Ile Gln Tyr Val Asp Tyr Phe  
                                   85                                  90                                  95

15 His Ala Leu Asp Ser Val Lys Leu Ala Gly Glu Ile Gln Lys Arg Ser  
                                   100                                  105                                  110

Asp Arg Val Ile Lys Cys Phe Leu Gln Val Asn Ile Ser Lys Glu Glu  
                   115                                  120                                  125

20 Ser Lys His Gly Phe Ser Arg Glu Glu Leu Leu Glu Ile Leu Pro Glu  
                   130                                  135                                  140

Leu Ala Gly Leu Asp Lys Ile Glu Tyr Val Gly Leu Met Thr Met Ala  
                   145                                  150                                  155                                  160

25 Pro Phe Glu Ala Ser Ser Glu Gln Leu Lys Glu Ile Phe Lys Ala Ala  
                                   165                                  170                                  175

30 Gln Asp Leu Gln Arg Glu Ile Gln Glu Lys Gln Ile Pro Asn Ile Pro  
                                   180                                  185                                  190

Met Thr Glu Leu Ser Met Gly Met Ser Arg Asp Tyr Lys Glu Ala Ile  
                   195                                  200                                  205

35 Gln Phe Gly Ser Thr Phe Val Arg Ile Gly Thr Ser Phe Phe Lys  
                   210                                  215                                  220

40 <210> 128  
     <211> 279  
     <212> PRT  
     <213> Streptococcus pneumoniae

45 <400> 128  
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                   1                                  5                                  10                                  15

Pro Leu Ala Ser Ala Ala Leu Ser Asp Val Ser Leu Thr Ile Glu Asp  
                                   20                                  25                                  30

50 Gly Ser Tyr Thr Ala Leu Ile Gly His Thr Gly Ser Gly Lys Ser Thr  
                   35                                  40                                  45

55 Ile Leu Gln Leu Leu Asn Gly Leu Leu Val Pro Ser Gln Gly Ser Val  
                   50                                  55                                  60

Arg Val Phe Asp Thr Leu Ile Thr Ser Thr Ser Lys Asn Lys Asp Ile

65                      70                      75                      80  
 Arg Gln Ile Arg Lys Gln Val Gly Leu Val Phe Gln Phe Ala Glu Asn  
                                  85                      90                      95  
 5    Gln Ile Phe Glu Glu Thr Val Leu Lys Asp Val Ala Phe Gly Pro Gln  
                                  100                      105                      110  
 10    Asn Phe Gly Val Ser Glu Glu Asp Ala Val Lys Thr Ala Arg Glu Lys  
                                  115                      120                      125  
       Leu Ala Leu Val Gly Ile Asp Glu Ser Leu Phe Asp Arg Ser Pro Phe  
                                  130                      135                      140  
 15    Glu Leu Ser Gly Gly Gln Met Arg Arg Val Ala Ile Ala Gly Ile Leu  
                                  145                      150                      155                      160  
       Ala Met Glu Pro Ala Ile Leu Val Leu Asp Glu Pro Thr Ala Gly Leu  
                                  165                      170                      175  
 20    Asp Pro Leu Gly Arg Lys Glu Leu Met Thr Leu Phe Lys Lys Leu His  
                                  180                      185                      190  
 25    Gln Ser Gly Met Thr Ile Val Leu Val Thr His Leu Met Asp Asp Val  
                                  195                      200                      205  
       Ala Glu Tyr Ala Asn Gln Val Tyr Val Met Glu Lys Gly Arg Leu Val  
                                  210                      215                      220  
 30    Lys Gly Gly Lys Pro Ser Asp Val Phe Gln Asp Val Val Phe Met Glu  
                                  225                      230                      235                      240  
       Glu Val Gln Leu Gly Val Pro Lys Ile Thr Ala Phe Cys Lys Arg Leu  
                                  245                      250                      255  
 35    Ala Asp Arg Gly Val Ser Phe Lys Arg Leu Pro Val Lys Ile Glu Glu  
                                  260                      265                      270  
 40    Phe Lys Glu Ser Leu Asn Gly  
                                  275  
  
 45    <210> 129  
       <211> 309  
       <212> PRT  
       <213> Streptococcus pneumoniae  
  
       <400> 129  
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       Arg Asn Val Ser Ser Leu Ala Leu Lys Leu Leu Asp Glu Ile Asn Glu  
                                  20                      25                      30  
 55    Val Trp Leu Phe Asp Cys Gly Glu Gly Thr Gln Asn Arg Ile Leu Glu  
                                  35                      40                      45

Thr Thr Ile Arg Pro Arg Lys Val Ser Lys Ile Phe Ile Thr His Leu  
 50 55 60  
 5 His Gly Asp His Ile Phe Gly Leu Pro Gly Phe Leu Ser Ser Arg Ala  
 65 70 75 80  
 Phe Gln Ala Asn Glu Glu Gln Thr Asp Leu Glu Ile Tyr Gly Pro Gln  
 85 90 95  
 10 Gly Ile Lys Ser Phe Val Leu Thr Ser Leu Arg Val Ser Gly Ser Arg  
 100 105 110  
 Leu Pro Tyr Arg Ile His Phe His Glu Phe Asp Gln Asp Ser Leu Gly  
 115 120 125  
 15 Lys Ile Leu Glu Ile Asp Lys Phe Thr Val Tyr Ala Glu Glu Leu Asp  
 130 135 140  
 20 His Thr Ile Phe Cys Val Gly Tyr Arg Val Met Gln Lys Asp Leu Glu  
 145 150 155 160  
 Gly Thr Leu Asp Ala Glu Lys Leu Lys Ala Ala Gly Val Pro Phe Gly  
 165 170 175  
 25 Pro Leu Phe Gly Lys Ile Lys Asn Gly Gln Asp Leu Val Leu Glu Asp  
 180 185 190  
 Gly Thr Glu Ile Lys Ala Ala Asp Tyr Ile Ser Ala Pro Arg Pro Gly  
 195 200 205  
 30 Lys Ile Ile Thr Ile Leu Gly Asp Thr Arg Lys Thr Asp Ala Ser Val  
 210 215 220  
 35 Arg Leu Ala Val Asn Ala Asp Val Leu Val His Glu Ser Thr Tyr Gly  
 225 230 235 240  
 Lys Gly Asp Glu Lys Ile Ala Arg Asn His Gly His Ser Thr Asn Met  
 245 250 255  
 40 Gln Ala Ala Gln Val Ala Val Glu Ala Gly Ala Lys Arg Leu Leu Leu  
 260 265 270  
 Asn His Ile Ser Ala Arg Phe Leu Ser Lys Asp Ile Ser Lys Leu Lys  
 275 280 285  
 45 Lys Asp Ala Ala Thr Ile Phe Glu Asn Val His Val Val Lys Asp Leu  
 290 295 300  
 50 Glu Glu Val Glu Ile  
 305  
 <210> 130  
 <211> 553  
 55 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 130  
 Met Ser Asn Ile Ser Leu Thr Thr Leu Gly Gly Val Arg Glu Asn Gly  
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 5 Lys Asn Met Tyr Ile Ala Glu Ile Gly Glu Ser Ile Phe Val Leu Asn  
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 Val Gly Leu Lys Tyr Pro Glu Asn Glu Gln Leu Gly Val Asp Val Val  
 35 40 45  
 10 Ile Pro Asn Met Asp Tyr Leu Phe Glu Asn Ser Asp Arg Ile Ala Gly  
 50 55 60  
 Val Phe Leu Thr His Gly His Ala Asp Ala Ile Gly Ala Leu Pro Tyr  
 15 65 70 75 80  
 Leu Leu Ala Glu Ala Lys Val Pro Val Phe Gly Ser Glu Leu Thr Ile  
 85 90 95  
 20 Glu Leu Ala Lys Leu Phe Val Lys Gly Asn Asp Ala Val Lys Lys Phe  
 100 105 110  
 Asn Asp Phe His Val Ile Asp Glu Asn Thr Glu Ile Asp Phe Gly Gly  
 115 120 125  
 25 Thr Val Val Ser Phe Phe Pro Thr Thr Tyr Ser Val Pro Glu Ser Leu  
 130 135 140  
 Gly Ile Val Leu Lys Thr Ser Glu Gly Ser Ile Val Tyr Thr Gly Asp  
 145 150 155 160  
 Phe Lys Phe Asp Gln Thr Ala Ser Glu Ser Tyr Ala Thr Asp Phe Ala  
 165 170 175  
 35 Arg Leu Ala Glu Ile Gly Arg Asp Gly Val Leu Ala Leu Leu Ser Asp  
 180 185 190  
 Ser Ala Asn Ala Asp Ser Asn Ile Gln Val Ala Ser Glu Ser Glu Val  
 195 200 205  
 40 Arg Asp Glu Ile Thr Gln Thr Ile Ala Asp Trp Glu Gly Arg Ile Ile  
 210 215 220  
 Val Ala Ala Val Ser Ser Asn Leu Ser Arg Ile Gln Gln Ile Phe Asp  
 225 230 235 240  
 Ala Ala Asp Lys Thr Gly Arg Arg Ile Val Leu Thr Gly Phe Asp Ile  
 245 250 255  
 50 Glu Asn Ile Val Arg Thr Ala Ile Arg Leu Lys Lys Leu Ser Leu Ala  
 260 265 270  
 Asn Glu Ile Leu Leu Ile Lys Pro Lys Asp Met Ser Arg Phe Glu Asp  
 275 280 285  
 55 His Glu Leu Ile Ile Leu Glu Thr Gly Arg Met Gly Glu Pro Ile Asn  
 290 295 300

Gly Leu Arg Lys Met Ser Ile Gly Arg His Arg Tyr Val Glu Ile Lys  
 305 310 315 320  
 5 Asp Gly Asp Leu Val Tyr Ile Ala Thr Ala Pro Ser Ile Ala Lys Glu  
 325 330 335  
 Ala Phe Val Ala Arg Val Glu Asn Met Ile Tyr Gln Ala Gly Gly Val  
 340 345 350  
 10 Val Lys Leu Ile Thr Gln Ser Leu His Val Ser Gly His Gly Asn Val  
 355 360 365  
 Arg Asp Leu Gln Leu Met Ile Asn Leu Leu Gln Pro Lys Tyr Leu Phe  
 15 370 375 380  
 Pro Val Gln Gly Glu Tyr Arg Glu Leu Asp Ala His Ala Lys Ala Ala  
 385 390 395 400  
 20 Met Ala Val Gly Met Leu Pro Glu Arg Ile Phe Ile Pro Lys Lys Gly  
 405 410 415  
 Thr Thr Met Ala Tyr Glu Asn Gly Asp Phe Val Pro Ala Gly Ser Val  
 420 425 430  
 25 Ser Ala Gly Asp Ile Leu Ile Asp Gly Asn Ala Ile Gly Asp Val Gly  
 435 440 445  
 Asn Val Val Leu Arg Asp Arg Lys Val Leu Ser Glu Asp Gly Ile Phe  
 30 450 455 460  
 Ile Val Ala Ile Thr Val Asn Arg Arg Glu Lys Lys Ile Val Ala Arg  
 465 470 475 480  
 35 Ala Arg Val His Thr Arg Gly Phe Val Tyr Leu Lys Lys Ser Arg Asp  
 485 490 495  
 Ile Leu Arg Glu Ser Ser Glu Leu Ile Asn Gln Thr Val Glu Asp Tyr  
 500 505 510  
 40 Leu Gln Gly Asp Asp Phe Asp Trp Ala Asp Leu Lys Gly Lys Val Arg  
 515 520 525  
 Asp Asn Leu Thr Lys Tyr Leu Phe Asp Gln Thr Lys Arg Arg Pro Ala  
 45 530 535 540  
 Ile Leu Pro Val Val Met Glu Ala Lys  
 545 550  
 50  
 <210> 131  
 <211> 316  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 55  
 <400> 131  
 Met Thr Lys Glu Phe His His Val Thr Val Leu Leu His Glu Thr Ile

|    |     |     |     |     |     |     |     |
|----|-----|-----|-----|-----|-----|-----|-----|
|    | 1   |     | 5   |     | 10  |     | 15  |
|    | Asp | Met | Leu | Asp | Val | Lys | Pro |
|    |     |     | 20  |     |     |     | 25  |
|    |     |     |     |     |     |     | 30  |
| 5  | Gly | Gly | Ala | Gly | His | Ser | Glu |
|    |     |     | 35  |     |     |     | 40  |
|    |     |     |     |     |     |     | 45  |
|    | Gly | His | Leu | Tyr | Ala | Phe | Asp |
| 10 |     |     | 50  |     |     |     | 55  |
|    |     |     |     |     |     |     | 60  |
|    | Gln | Lys | Arg | Leu | Ala | Pro | Tyr |
|    |     |     | 65  |     |     |     | 70  |
|    |     |     |     |     |     |     | 75  |
|    |     |     |     |     |     |     | 80  |
| 15 | Lys | Asp | Asn | Phe | Arg | His | Leu |
|    |     |     |     |     |     |     | 85  |
|    |     |     |     |     |     |     | 90  |
|    | Gln | Glu | Ile | Asp | Gly | Ile | Cys |
|    |     |     | 100 |     |     |     | 105 |
| 20 |     |     |     |     |     |     | 110 |
|    | Leu | Asp | Gln | Arg | Glu | Arg | Gly |
|    |     |     | 115 |     |     |     | 120 |
|    |     |     |     |     |     |     | 125 |
|    | Asp | Met | Arg | Met | Asn | Gln | Asp |
| 25 |     |     | 130 |     |     |     | 135 |
|    |     |     |     |     |     |     | 140 |
|    | Asn | His | Tyr | Asp | Tyr | His | Asp |
|    |     |     | 145 |     |     |     | 150 |
|    |     |     |     |     |     |     | 155 |
|    |     |     |     |     |     |     | 160 |
| 30 | Glu | Asp | Lys | Phe | Ser | Lys | Gln |
|    |     |     |     |     |     |     | 165 |
|    |     |     |     |     |     |     | 170 |
|    |     |     |     |     |     |     | 175 |
|    | Glu | Val | Lys | Pro | Ile | Glu | Thr |
|    |     |     | 180 |     |     |     | 185 |
| 35 |     |     |     |     |     |     | 190 |
|    | Leu | Val | Lys | Pro | Ala | Lys | Glu |
|    |     |     | 195 |     |     |     | 200 |
|    |     |     |     |     |     |     | 205 |
|    | Gln | Ile | Phe | Gln | Ala | Ile | Arg |
| 40 |     |     | 210 |     |     |     | 215 |
|    |     |     |     |     |     |     | 220 |
|    | Ala | Asp | Glu | Ser | Ile | Gln | Gln |
|    |     |     | 225 |     |     |     | 230 |
|    |     |     |     |     |     |     | 235 |
|    |     |     |     |     |     |     | 240 |
| 45 | Arg | Ile | Ser | Val | Ile | Thr | Phe |
|    |     |     |     |     |     |     | 245 |
|    |     |     |     |     |     |     | 250 |
|    |     |     |     |     |     |     | 255 |
|    | Gln | Leu | Phe | Lys | Glu | Ala | Ser |
|    |     |     | 260 |     |     |     | 265 |
| 50 |     |     |     |     |     |     | 270 |
|    | Phe | Ile | Pro | Asp | Asp | Leu | Lys |
|    |     |     | 275 |     |     |     | 280 |
|    |     |     |     |     |     |     | 285 |
|    | Pro | Ile | Leu | Pro | Ser | Ala | Glu |
| 55 |     |     | 290 |     |     |     | 295 |
|    |     |     |     |     |     |     | 300 |
|    | Ser | Ala | Lys | Leu | Arg | Val | Val |
|    |     |     |     |     |     |     | Arg |
|    |     |     |     |     |     |     | Lys |
|    |     |     |     |     |     |     | Ile |
|    |     |     |     |     |     |     | His |
|    |     |     |     |     |     |     | Lys |

70



Gly Leu Asp Tyr Val Asp Gln Lys Ile Leu Arg Thr Met Ile Glu Met  
 260 265 270  
 5 Tyr Ser Gly Gly Pro Val Gly Leu Gly Thr Leu Ser Val Asn Ile Ala  
 275 280 285  
 Glu Glu Arg Glu Thr Val Glu Asp Met Tyr Glu Pro Tyr Leu Ile Gln  
 290 295 300  
 10 Lys Gly Phe Ile Met Arg Thr Arg Ser Gly Arg Val Ala Thr Ala Lys  
 305 310 315 320  
 Ala Tyr Glu His Leu Gly Tyr Glu Tyr Ser Glu Lys  
 325 330  
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 <212> PRT  
 20 <213> Streptococcus pneumoniae  
 <400> 133  
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 20 25 30  
 Gly Gly Pro Trp Gly Gly Asp Gly Gly Arg Gly Gly Asn Val Val Phe  
 30 35 40 45  
 Val Val Asp Glu Gly Leu Arg Thr Leu Met Asp Phe Arg Tyr Asn Arg  
 50 55 60  
 35 His Phe Lys Ala Asp Ser Gly Glu Lys Gly Met Thr Lys Gly Met His  
 65 70 75 80  
 Gly Arg Gly Ala Glu Asp Leu Arg Val Arg Val Ser Gln Gly Thr Thr  
 85 90 95  
 40 Val Arg Asp Ala Glu Thr Gly Lys Val Leu Thr Asp Leu Ile Lys His  
 100 105 110  
 Gly Gln Glu Phe Ile Val Ala His Gly Gly Arg Gly Gly Arg Gly Asn  
 115 120 125  
 45 Ile Arg Phe Ala Thr Pro Lys Asn Pro Ala Pro Glu Ile Ser Glu Asn  
 130 135 140  
 50 Gly Glu Pro Gly Gln Glu Arg Glu Leu Gln Leu Glu Leu Lys Ile Leu  
 145 150 155 160  
 Ala Asp Val Gly Leu Val Gly Phe Pro Ser Val Gly Lys Ser Thr Leu  
 165 170 175  
 55 Leu Ser Val Ile Thr Ser Ala Lys Pro Lys Ile Gly Ala Tyr His Phe  
 180 185 190

Thr Thr Ile Val Pro Asn Leu Gly Met Val Arg Thr Gln Ser Gly Glu  
 195 200 205  
 5 Ser Phe Ala Val Ala Asp Leu Pro Gly Leu Ile Glu Gly Ala Ser Gln  
 210 215 220  
 Gly Val Gly Leu Gly Thr Gln Phe Leu Arg His Ile Glu Arg Thr Arg  
 225 230 235 240  
 10 Val Ile Leu His Ile Ile Asp Met Ser Ala Ser Glu Gly Arg Asp Pro  
 245 250 255  
 15 Tyr Glu Asp Tyr Leu Ala Ile Asn Lys Glu Leu Glu Ser Tyr Asn Leu  
 260 265 270  
 Arg Leu Met Glu Arg Pro Gln Ile Ile Val Ala Asn Lys Met Asp Met  
 275 280 285  
 20 Pro Glu Ser Gln Glu Asn Leu Glu Glu Phe Lys Lys Lys Leu Ala Glu  
 290 295 300  
 Asn Tyr Asp Glu Phe Glu Glu Leu Pro Ala Ile Phe Pro Ile Ser Gly  
 305 310 315 320  
 25 Leu Thr Lys Gln Gly Leu Ala Thr Leu Leu Asp Ala Thr Ala Glu Leu  
 325 330 335  
 30 Leu Asp Lys Thr Pro Glu Phe Leu Leu Tyr Asp Glu Ser Asp Met Glu  
 340 345 350  
 Glu Glu Ala Tyr Tyr Gly Phe Asp Glu Glu Glu Lys Ala Phe Glu Ile  
 355 360 365  
 35 Ser Arg Asp Asp Asp Ala Thr Trp Val Leu Ser Gly Glu Lys Leu Met  
 370 375 380  
 Lys Leu Phe Asn Met Thr Asn Phe Asp Arg Asp Glu Ser Val Met Lys  
 385 390 395 400  
 40 Phe Ala Arg Gln Leu Arg Gly Met Gly Val Asp Glu Ala Leu Arg Ala  
 405 410 415  
 45 Arg Gly Ala Lys Asp Gly Asp Leu Val Arg Ile Gly Lys Phe Glu Phe  
 420 425 430  
 Glu Phe Val Asp  
 435  
 50  
 <210> 134  
 <211> 172  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 55  
 <400> 134  
 Met Asn Tyr Phe Asn Val Gly Lys Ile Val Asn Thr Gln Gly Leu Gln

73

Leu Ala Gln Glu Glu Glu Leu Ile Phe Ile Cys Gly His Tyr Glu Gly  
 100 105 110  
 5 Tyr Asp Glu Arg Ile Lys Thr Leu Val Thr Asp Glu Ile Ser Leu Gly  
 115 120 125  
 Asp Tyr Val Leu Thr Gly Gly Glu Leu Ala Ala Met Thr Met Ile Asp  
 130 135 140  
 10 Ala Thr Val Arg Leu Ile Pro Glu Val Ile Gly Lys Glu Ser Ser His  
 145 150 155 160  
 Gln Asp Asp Ser Phe Ser Ser Gly Leu Leu Glu Tyr His Gln Tyr Thr  
 165 170 175  
 15 Arg Pro Tyr Asp Tyr Arg Gly Met Val Val Pro Asp Val Leu Met Ser  
 180 185 190  
 20 Gly His His Glu Lys Ile Arg Gln Trp Arg Leu Tyr Glu Ser Leu Lys  
 195 200 205  
 Lys Thr Tyr Glu Arg Arg Pro Asp Leu Leu Glu His Tyr Gln Leu Thr  
 210 215 220  
 25 Val Glu Glu Glu Lys Met Leu Ala Glu Ile Lys Glu Asn Lys Glu  
 225 230 235  
 30  
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 35 <213> Streptococcus pneumoniae  
 <400> 136  
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 Asp Gly Lys Leu Ile Arg Val Leu Glu Ala Ser His His Lys Pro Gly  
 20 25 30  
 45 Lys Gly Asn Thr Ile Met Arg Met Lys Leu Arg Asp Val Arg Thr Gly  
 35 40 45  
 Ser Thr Phe Asp Thr Ser Tyr Arg Pro Glu Glu Lys Phe Glu Gln Ala  
 50 55 60  
 50 Ile Ile Glu Thr Val Pro Ala Gln Tyr Leu Tyr Lys Met Asp Asp Thr  
 65 70 75 80  
 Ala Tyr Phe Met Asn Thr Glu Thr Tyr Asp Gln Tyr Glu Ile Pro Val  
 55 85 90 95  
 Val Asn Val Glu Asn Glu Leu Leu Tyr Ile Leu Glu Asn Ser Asp Val

100 105 110  
 Lys Ile Gln Phe Tyr Gly Thr Glu Val Ile Gly Val Thr Val Pro Thr  
 115 120 125  
 5 Thr Val Glu Leu Thr Val Ala Glu Thr Gln Pro Ser Ile Lys Gly Ala  
 130 135 140  
 10 Thr Val Thr Gly Ser Gly Lys Pro Ala Thr Met Glu Thr Gly Leu Val  
 145 150 155 160  
 Val Asn Val Pro Asp Phe Ile Glu Ala Gly Gln Lys Leu Val Ile Asn  
 165 170 175  
 15 Thr Ala Glu Gly Thr Tyr Val Ser Arg Ala  
 180 185  
 20 <210> 137  
 <211> 523  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 25 <400> 137  
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 20 25 30  
 Lys Glu Ile Arg Leu Ala Leu Leu Glu Ala Asp Val Ala Leu Pro Val  
 35 40 45  
 35 Val Lys Asp Phe Ile Lys Lys Val Arg Glu Arg Ala Val Gly His Glu  
 50 55 60  
 Val Ile Asp Thr Leu Asn Pro Ala Gln Gln Ile Ile Lys Ile Val Asp  
 65 70 75 80  
 40 Glu Glu Leu Thr Ala Val Leu Gly Ser Asp Thr Ala Glu Ile Ile Lys  
 85 90 95  
 45 Ser Pro Lys Ile Pro Thr Ile Ile Met Met Val Gly Leu Gln Gly Ala  
 100 105 110  
 Gly Lys Thr Thr Phe Ala Gly Lys Leu Ala Asn Lys Leu Lys Lys Glu  
 115 120 125  
 50 Glu Asn Ala Arg Pro Leu Met Ile Ala Ala Asp Ile Tyr Arg Pro Ala  
 130 135 140  
 Ala Ile Asp Gln Leu Lys Thr Leu Gly Gln Gln Ile Asp Val Pro Val  
 145 150 155 160  
 55 Phe Ala Leu Gly Thr Glu Val Pro Ala Val Glu Ile Val Arg Gln Gly  
 165 170 175

Leu Glu Gln Ala Gln Thr Asn His Asn Asp Tyr Val Leu Ile Asp Thr  
 180 185 190  
 5 Ala Gly Arg Leu Gln Ile Asp Glu Leu Leu Met Asn Glu Leu Arg Asp  
 195 200 205  
 Val Lys Thr Leu Ala Gln Pro Asn Glu Ile Leu Leu Val Val Asp Ala  
 210 215 220  
 10 Met Ile Gly Gln Glu Ala Ala Asn Val Ala Arg Glu Phe Asn Ala Gln  
 225 230 235 240  
 Leu Glu Val Thr Gly Val Ile Leu Thr Lys Ile Asp Gly Asp Thr Arg  
 15 245 250 255  
 Gly Gly Ala Ala Leu Ser Val Arg His Ile Thr Gly Lys Pro Ile Lys  
 260 265 270  
 20 Phe Thr Gly Thr Gly Glu Lys Ile Thr Asp Ile Glu Thr Phe His Pro  
 275 280 285  
 Asp Arg Met Ser Ser Arg Ile Leu Gly Met Gly Asp Met Leu Thr Leu  
 25 290 295 300  
 Ile Glu Lys Ala Ser Gln Glu Tyr Asp Glu Gln Lys Ala Leu Glu Met  
 305 310 315 320  
 Ala Glu Lys Met Arg Glu Asn Thr Phe Asp Phe Asn Asp Phe Ile Asp  
 30 325 330 335  
 Gln Leu Asp Gln Val Gln Asn Met Gly Pro Met Glu Asp Leu Leu Lys  
 340 345 350  
 35 Met Ile Pro Gly Met Ala Asn Asn Pro Ala Leu Gln Asn Met Lys Val  
 355 360 365  
 Asp Glu Arg Gln Ile Ala Arg Lys Arg Ala Ile Val Ser Ser Met Thr  
 370 375 380  
 40 Pro Glu Glu Arg Glu Asn Pro Asp Leu Leu Asn Pro Ser Arg Arg Arg  
 385 390 395 400  
 Arg Ile Ala Ala Gly Ser Gly Asn Thr Phe Val Glu Val Asn Lys Phe  
 45 405 410 415  
 Ile Lys Asp Phe Asn Gln Ala Lys Gln Leu Met Gln Gly Val Met Ser  
 420 425 430  
 50 Gly Asp Met Asn Lys Met Met Lys Gln Met Gly Ile Asn Pro Asn Asn  
 435 440 445  
 Leu Pro Lys Asn Met Pro Asn Met Gly Gly Met Asp Met Ser Ala Leu  
 450 455 460  
 55 Glu Gly Met Met Gly Gln Gly Gly Met Pro Asp Leu Ser Ala Leu Gly  
 465 470 475 480

Gly Ala Gly Met Pro Asp Met Ser Gln Met Phe Gly Gly Gly Leu Lys  
 485 490 495  
 5 Gly Lys Ile Gly Glu Phe Ala Met Lys Gln Ser Met Lys Arg Met Ala  
 500 505 510  
 Asn Lys Met Lys Lys Ala Lys Lys Lys Arg Lys  
 515 520  
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 <211> 281  
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 15 <213> Streptococcus pneumoniae  
 <400> 138  
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 20 25 30  
 Ala Glu Glu Phe Ile Gln Tyr Gln Asn Gln Asn Glu Ala Phe Met Ser  
 35 40 45  
 25 Met Phe Asn Val Val Ile Gln Leu Gly Ala Ile Leu Ala Val Met Val  
 50 55 60  
 30 Ile Tyr Phe Asn Lys Leu Asn Pro Phe Lys Pro Thr Lys Asp Lys Gln  
 65 70 75 80  
 Glu Val Arg Lys Thr Trp Arg Leu Trp Leu Lys Val Leu Ile Ala Thr  
 85 90 95  
 35 Leu Pro Leu Leu Gly Val Phe Lys Phe Asp Asp Trp Phe Asp Thr His  
 100 105 110  
 Phe His Asn Met Val Ser Val Ala Leu Met Leu Ile Ile Tyr Gly Val  
 115 120 125  
 40 Ala Phe Ile Tyr Leu Glu Lys Arg Asn Lys Ala Arg Ala Ile Glu Pro  
 130 135 140  
 45 Ser Val Thr Glu Leu Asp Lys Leu Pro Tyr Thr Thr Ala Phe Tyr Ile  
 145 150 155 160  
 Gly Leu Phe Gln Val Leu Ala Leu Leu Pro Gly Thr Ser Arg Ser Gly  
 165 170 175  
 50 Ala Thr Ile Val Gly Gly Leu Leu Asn Gly Thr Ser Arg Ser Val Val  
 180 185 190  
 55 Thr Glu Phe Thr Phe Tyr Leu Gly Ile Pro Val Met Phe Gly Ala Ser  
 195 200 205  
 Ala Leu Lys Ile Phe Lys Phe Val Lys Ala Gly Glu Leu Leu Ser Phe

210                      215                      220  
 Gly Gln Leu Phe Leu Leu Leu Val Ala Met Gly Val Ala Phe Ala Val  
 225                      230                      235                      240  
 5 Ser Met Val Ala Ile Arg Phe Leu Thr Ser Tyr Val Lys Lys His Asp  
                     245                      250                      255  
 10 Phe Thr Leu Phe Gly Lys Tyr Arg Ile Val Leu Gly Ser Val Leu Leu  
                     260                      265                      270  
 Leu Tyr Ser Phe Val Arg Leu Phe Val  
                     275                      280  
 15  
 <210> 139  
 <211> 429  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 20  
 <400> 139  
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 25 Glu Glu Val Val Lys Glu Ala Leu Glu Asn Leu Asp Leu Ser Glu Asp  
                     20                      25                      30  
 Ile Glu Pro Ala Phe Thr Glu Ala Glu Glu Val Ser Gln Glu Glu Ala  
                     35                      40                      45  
 30 Glu Val Glu Ser Ser Glu Glu Ser Val Phe Gln Glu Glu Asp Ser Gln  
                     50                      55                      60  
 35 Asp Thr Val Glu Glu Asn Leu Asp Leu Glu Pro Val Val Glu Val Ser  
                     65                      70                      75                      80  
 Gln Glu Glu Val Glu Glu Phe Pro Asn Ser Gln Glu Val Thr Glu Glu  
                     85                      90                      95  
 40 Glu Lys Leu Glu His Glu Gly Thr Val Glu Glu Asn Asn Phe Glu Val  
                     100                      105                      110  
 Leu Glu Pro Glu Ala Pro Gln Thr Glu Glu Thr Val Gln Glu Lys Tyr  
                     115                      120                      125  
 45 Asp Arg Ser Leu Lys Lys Thr Arg Thr Gly Phe Gly Ala Arg Leu Asn  
                     130                      135                      140  
 50 Ala Phe Phe Ala Asn Phe Arg Ser Val Asp Glu Glu Phe Phe Glu Glu  
                     145                      150                      155                      160  
 Leu Glu Glu Leu Leu Ile Met Ser Asp Val Gly Val Gln Val Ala Ser  
                     165                      170                      175  
 55 Asn Leu Thr Glu Glu Leu Arg Tyr Glu Ala Lys Leu Glu Asn Ala Lys  
                     180                      185                      190



Lys Pro Asp Ala Leu Arg Arg Val Ile Ile Glu Lys Leu Val Glu Leu  
 195 200 205  
 5 Tyr Glu Lys Asp Gly Ser Tyr Asp Glu Ser Ile His Phe Gln Asp Asn  
 210 215 220  
 Leu Thr Val Met Leu Phe Val Gly Val Asn Gly Val Gly Lys Thr Thr  
 225 230 235 240  
 10 Ser Ile Gly Lys Leu Ala His Arg Tyr Lys Arg Ala Gly Lys Lys Val  
 245 250 255  
 Met Leu Val Ala Ala Asp Thr Phe Arg Ala Gly Ala Val Ala Gln Leu  
 260 265 270  
 15 Ala Glu Trp Gly Arg Arg Val Asp Val Pro Val Val Thr Gly Pro Glu  
 275 280 285  
 20 Lys Ala Asp Pro Ala Ser Val Val Phe Asp Gly Met Glu Arg Ala Val  
 290 295 300  
 Ala Glu Gly Ile Asp Ile Leu Met Ile Asp Thr Ala Gly Arg Leu Gln  
 305 310 315 320  
 25 Asn Lys Asp Asn Leu Met Ala Glu Leu Glu Lys Ile Gly Arg Ile Ile  
 325 330 335  
 Lys Arg Val Val Pro Glu Ala Pro His Glu Thr Phe Leu Ala Leu Asp  
 340 345 350  
 30 Ala Ser Thr Gly Gln Asn Ala Leu Val Gln Ala Lys Glu Phe Ser Lys  
 355 360 365  
 35 Ile Thr Pro Leu Thr Gly Ile Val Leu Thr Lys Ile Asp Gly Thr Ala  
 370 375 380  
 Arg Gly Gly Val Val Leu Ala Ile Arg Glu Glu Leu Asn Ile Pro Val  
 385 390 395 400  
 40 Lys Leu Ile Gly Phe Gly Glu Lys Ile Asp Asp Ile Gly Glu Phe Asn  
 405 410 415  
 Ser Glu Asn Phe Met Lys Gly Leu Leu Glu Gly Leu Ile  
 420 425  
 45  
 <210> 140  
 <211> 165  
 <212> PRT  
 50 <213> Streptococcus pneumoniae  
 <400> 140  
 Met Tyr Ile Glu Met Val Asp Glu Thr Gly Gln Val Ser Lys Glu Met  
 1 5 10 15  
 55 Leu Gln Gln Thr Gln Glu Ile Leu Glu Phe Ala Ala Lys Lys Leu Gly  
 20 25 30

Lys Glu Asp Lys Glu Met Ala Val Thr Phe Val Thr Asn Glu Arg Ser  
                   35                                  40                                  45

5 His Glu Leu Asn Leu Glu Tyr Arg Asp Thr Asp Arg Pro Thr Asp Val  
                   50                                  55                                  60

Ile Ser Leu Glu Tyr Lys Pro Glu Leu Glu Ile Ala Phe Asp Glu Glu  
                   65                                  70                                  75                                  80

10 Asp Leu Leu Glu Asn Pro Glu Leu Ala Glu Met Met Ser Glu Phe Asp  
                                   85                                  90                                  95

Ala Tyr Ile Gly Glu Leu Phe Ile Ser Ile Asp Lys Ala His Glu Gln  
                   100                                  105                                  110

15 Ala Glu Glu Tyr Gly His Ser Phe Glu Arg Glu Met Gly Phe Leu Ala  
                   115                                  120                                  125

20 Val His Gly Phe Leu His Ile Asn Gly Tyr Asp His Tyr Thr Pro Glu  
                   130                                  135                                  140

Glu Glu Ala Glu Met Phe Gly Leu Gln Glu Glu Ile Leu Thr Ala Tyr  
                   145                                  150                                  155                                  160

25 Gly Leu Thr Arg Gln  
                                   165

30 <210> 141  
       <211> 255  
       <212> PRT  
       <213> Streptococcus pneumoniae

35 <400> 141  
       Met Ser Ile Arg Val Ile Ile Ala Gly Phe Lys Gly Lys Met Gly Gln  
           1                                  5                                  10                                  15

40 Ala Ala Cys Gln Met Val Leu Thr Asp Pro Asp Leu Asp Leu Val Ala  
                   20                                  25                                  30

Val Leu Asp Pro Phe Glu Ser Glu Ser Glu Trp Gln Gly Ile Pro Val  
                   35                                  40                                  45

45 Phe Lys Asp Lys Ala Asp Leu Ala Gly Phe Glu Ala Asp Val Trp Val  
                   50                                  55                                  60

Asp Phe Thr Thr Pro Ala Val Ala Tyr Glu Asn Thr Arg Phe Ala Leu  
                   65                                  70                                  75                                  80

50 Glu Asn Gly Phe Ala Pro Val Val Gly Thr Thr Gly Phe Thr Ser Glu  
                                   85                                  90                                  95

Glu Ile Ala Glu Leu Lys Glu Phe Ser Arg Ala Gln Asp Leu Gly Gly  
                   100                                  105                                  110

55 Leu Ile Ala Pro Asn Phe Ala Leu Gly Ala Val Leu Leu Met Gln Phe

115                      120                      125  
 Ala Thr Gln Ala Ala Lys Tyr Phe Pro Asn Val Glu Ile Ile Glu Leu  
 130                      135                      140  
 5 His His Asp Lys Lys Lys Asp Ala Pro Ser Gly Thr Ala Ile Lys Thr  
 145                      150                      155                      160  
 Ala Glu Leu Met Ala Glu Val Arg Glu Ser Ile Gln Gln Gly Ala Ala  
 10                      165                      170                      175  
 Asp Glu Glu Glu Leu Ile Ala Gly Ala Arg Gly Ala Asp Phe Asp Gly  
 180                      185                      190  
 15 Met Arg Ile His Ser Val Arg Leu Pro Gly Leu Val Ala His Gln Glu  
 195                      200                      205  
 Val Ile Phe Gly Asn Gln Gly Glu Gly Leu Thr Leu Arg His Asp Ser  
 20                      210                      215                      220  
 Tyr Asp Arg Ile Ser Phe Met Thr Gly Val Asn Leu Gly Ile Lys Glu  
 225                      230                      235                      240  
 25 Val Val Lys Arg His Glu Leu Val Tyr Gly Leu Glu His Leu Leu  
 245                      250                      255  
  
 <210> 142  
 <211> 91  
 30 <212> PRT  
 <213> Streptococcus pneumoniae  
  
 <400> 142  
 35 Met Ala Asn Lys Gln Asp Leu Ile Ala Lys Val Ala Glu Ala Thr Glu  
 1                      5                      10                      15  
 Leu Thr Lys Lys Asp Ser Ala Ala Ala Val Glu Ala Val Phe Ala Ala  
 20                      25                      30  
 40 Val Ala Asp Tyr Leu Ala Ala Gly Glu Lys Val Gln Leu Ile Gly Phe  
 35                      40                      45  
 Ser Asn Phe Glu Val Arg Glu Arg Ala Glu Arg Lys Gly Arg Asn Pro  
 50                      55                      60  
 45 Gln Thr Gly Lys Glu Met Thr Ile Ala Ala Ser Lys Val Pro Ala Phe  
 65                      70                      75                      80  
 Lys Ala Gly Lys Ala Leu Lys Asp Ala Val Lys  
 50                      85                      90  
  
 <210> 143  
 <211> 306  
 55 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 143  
 Met Thr Lys Thr Ala Phe Leu Phe Ala Gly Gln Gly Ala Gln Tyr Leu  
 1 5 10 15

5 Gly Met Gly Arg Asp Phe Tyr Asp Gln Tyr Pro Ile Val Lys Glu Thr  
 20 25 30

Ile Asp Arg Ala Ser Gln Val Leu Gly Tyr Asp Leu Arg Tyr Leu Ile  
 35 40 45

10 Asp Thr Glu Glu Asp Lys Leu Asn Gln Thr Arg Tyr Thr Gln Pro Ala  
 50 55 60

Ile Leu Ala Thr Ser Val Ala Ile Tyr Arg Leu Leu Gln Glu Lys Gly  
 65 70 75 80

15 Tyr Gln Pro Asp Met Val Ala Gly Leu Ser Leu Gly Glu Tyr Ser Ala  
 85 90 95

20 Leu Val Ala Ser Gly Ala Leu Asp Phe Glu Asp Ala Val Ala Leu Val  
 100 105 110

Ala Lys Arg Gly Ala Tyr Met Glu Glu Ala Ala Pro Ala Asp Ser Gly  
 115 120 125

25 Lys Met Val Ala Val Leu Asn Thr Pro Val Glu Val Ile Glu Glu Ala  
 130 135 140

Cys Gln Lys Ala Ser Glu Leu Gly Val Val Thr Pro Ala Asn Tyr Asn  
 145 150 155 160

30 Thr Pro Ala Gln Ile Val Ile Ala Gly Glu Val Val Ala Val Asp Arg  
 165 170 175

35 Ala Val Glu Leu Leu Gln Glu Ala Gly Ala Lys Arg Leu Ile Pro Leu  
 180 185 190

Lys Val Ser Gly Pro Phe His Thr Ala Leu Leu Glu Pro Ala Ser Gln  
 195 200 205

40 Lys Leu Ala Glu Thr Leu Ala Gln Val Ser Phe Ser Asp Phe Thr Cys  
 210 215 220

Pro Leu Val Gly Asn Thr Glu Ala Ala Val Met Gln Lys Glu Asp Ile  
 225 230 235 240

45 Ala Gln Leu Leu Thr Arg Gln Val Lys Glu Pro Val Arg Phe Tyr Glu  
 245 250 255

50 Ser Ile Gly Val Met Gln Glu Ala Gly Ile Ser Asn Phe Ile Glu Ile  
 260 265 270

Gly Pro Gly Lys Val Leu Ser Gly Phe Val Lys Lys Ile Asp Gln Thr  
 275 280 285

55 Ala His Leu Ala His Val Glu Asp Gln Ala Ser Leu Val Ala Leu Leu  
 290 295 300

Glu Lys  
305

5  
<210> 144  
<211> 243  
<212> PRT  
<213> Streptococcus pneumoniae

10  
<400> 144  
Met Lys Leu Glu His Lys Asn Ile Phe Ile Thr Gly Ser Ser Arg Gly  
1 5 10 15

15 Ile Gly Leu Ala Ile Ala His Lys Phe Ala Gln Ala Gly Ala Asn Ile  
20 25 30

Val Leu Asn Ser Arg Gly Ala Ile Ser Glu Glu Leu Leu Ala Glu Phe  
35 40 45

20 Ser Asn Tyr Gly Ile Lys Val Val Pro Ile Ser Gly Asp Val Ser Asp  
50 55 60

Phe Ala Asp Ala Lys Arg Met Ile Asp Gln Ala Ile Ala Glu Leu Gly  
25 65 70 75 80

Ser Val Asp Val Leu Val Asn Asn Ala Gly Ile Thr Gln Asp Thr Leu  
85 90 95

30 Met Leu Lys Met Thr Glu Ala Asp Phe Glu Lys Val Leu Lys Val Asn  
100 105 110

Leu Thr Gly Ala Phe Asn Met Thr Gln Ser Val Leu Lys Pro Met Met  
115 120 125

35 Lys Ala Arg Glu Gly Ala Ile Ile Asn Met Ser Ser Val Val Gly Leu  
130 135 140

Met Gly Asn Ile Gly Gln Ala Asn Tyr Ala Ala Ser Lys Ala Gly Leu  
40 145 150 155 160

Ile Gly Phe Thr Lys Ser Val Ala Arg Glu Val Ala Ser Arg Asn Ile  
165 170 175

45 Arg Val Asn Val Ile Ala Pro Gly Met Ile Glu Ser Asp Met Thr Ala  
180 185 190

Ile Leu Ser Asp Lys Ile Lys Glu Ala Thr Leu Ala Gln Ile Pro Met  
195 200 205

50 Lys Glu Phe Gly Gln Ala Glu Gln Val Ala Asp Leu Thr Val Phe Leu  
210 215 220

Ala Gly Gln Asp Tyr Leu Thr Gly Gln Val Val Ala Ile Asp Gly Gly  
55 225 230 235 240

Leu Ser Met

5 <210> 145  
 <211> 276  
 <212> PRT  
 <213> Streptococcus pneumoniae  
  
 <400> 145  
 10 Met Gly Val Lys Lys Lys Leu Lys Leu Thr Ser Leu Leu Gly Leu Ser  
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     Leu Leu Ile Met Thr Ala Cys Ala Thr Asn Gly Val Thr Ser Asp Ile  
                     20                    25                    30  
 15 Thr Ala Glu Ser Ala Asp Phe Trp Ser Lys Leu Val Tyr Phe Phe Ala  
                     35                    40                    45  
  
     Glu Ile Ile Arg Phe Leu Ser Phe Asp Ile Ser Ile Gly Val Gly Ile  
 20                    50                    55                    60  
  
     Ile Leu Phe Thr Val Leu Ile Arg Thr Val Leu Leu Pro Val Phe Gln  
     65                    70                    75                    80  
  
 25 Val Gln Met Val Ala Ser Arg Lys Met Gln Glu Ala Gln Pro Arg Ile  
                     85                    90                    95  
  
     Lys Ala Leu Arg Glu Gln Tyr Pro Gly Arg Asp Met Glu Ser Arg Thr  
                     100                    105                    110  
 30 Lys Leu Glu Gln Glu Met Arg Lys Val Phe Lys Glu Met Gly Val Arg  
                     115                    120                    125  
  
     Gln Ser Asp Ser Leu Trp Pro Ile Leu Ile Gln Met Pro Val Ile Leu  
 35                    130                    135                    140  
  
     Ala Leu Phe Gln Ala Leu Ser Arg Val Asp Phe Leu Lys Thr Gly His  
     145                    150                    155                    160  
  
 40 Phe Leu Trp Ile Asn Leu Gly Ser Val Asp Thr Thr Leu Val Leu Pro  
                     165                    170                    175  
  
     Ile Leu Ala Ala Val Phe Thr Phe Leu Ser Thr Trp Leu Ser Asn Lys  
                     180                    185                    190  
 45 Ala Leu Ser Glu Arg Asn Gly Ala Thr Thr Ala Met Met Tyr Gly Ile  
                     195                    200                    205  
  
     Pro Val Leu Ile Phe Ile Phe Ala Val Tyr Ala Pro Gly Gly Val Ala  
 50                    210                    215                    220  
  
     Leu Tyr Trp Thr Val Ser Asn Ala Tyr Gln Val Leu Gln Thr Tyr Phe  
     225                    230                    235                    240  
  
 55 Leu Asn Asn Pro Phe Lys Ile Ile Ala Glu Arg Glu Ala Val Val Gln  
                     245                    250                    255

85

Ala Phe Phe Asn Pro Phe Ala Asp Arg Ala Asp Ala Gly His Gln Leu  
 245 250 255

5 Ala Asn Ser Tyr Phe Ala Met Val Asn Gly Gly Trp Phe Gly Leu Gly  
 260 265 270

Leu Gly Asn Ser Ile Glu Lys Arg Gly Tyr Leu Pro Glu Ala His Thr  
 275 280 285

10 Asp Phe Val Phe Ser Ile Val Ile Glu Glu Phe Gly Phe Val Gly Ala  
 290 295 300

15 Ser Leu Ile Leu Ala Leu Leu Phe Phe Met Ile Leu Arg Ile Ile Leu  
 305 310 315 320

Val Gly Ile Arg Ala Glu Asn Pro Phe Asn Ala Met Val Ala Leu Gly  
 325 330 335

20 Val Gly Gly Met Met Leu Val Gln Val Phe Val Asn Ile Gly Gly Ile  
 340 345 350

Ser Gly Leu Ile Pro Ser Thr Gly Val Thr Phe Pro Phe Leu Ser Gln  
 355 360 365

25 Gly Gly Asn Ser Leu Leu Val Leu Ser Val Ala Val Ala Phe Val Leu  
 370 375 380

30 Asn Ile Asp Ala Ser Glu Lys Arg Ala Lys Leu Tyr Arg Glu Leu Glu  
 385 390 395 400

Asn Gln Pro Met Asn Leu Leu Leu Lys  
 405

35 <210> 147  
 <211> 419  
 <212> PRT  
 <213> Streptococcus pneumoniae

40 <400> 147  
 Met Leu Gly Ile Leu Thr Phe Ile Leu Val Phe Gly Ile Ile Val Val  
 1 5 10 15

45 Val His Glu Phe Gly His Phe Tyr Phe Ala Lys Lys Ser Gly Ile Leu  
 20 25 30

Val Arg Glu Phe Ala Ile Gly Met Gly Pro Lys Ile Phe Ala His Ile  
 35 40 45

50 Gly Lys Asp Gly Thr Ala Tyr Thr Ile Arg Ile Leu Pro Leu Gly Gly  
 50 55 60

55 Tyr Val Arg Met Ala Gly Trp Gly Asp Asp Thr Thr Glu Ile Lys Thr  
 65 70 75 80

Gly Thr Pro Val Ser Leu Thr Leu Ala Asp Asp Gly Lys Val Lys Arg



|    | 85  | 90  | 95  |
|----|---|-----|-----|
|    | Ile Asn Leu Ser Gly Lys Lys Leu Asp Gln Thr Ala Leu Pro Met Gln |     |     |
|    | 100   | 105 | 110 |
| 5  | Val Thr Gln Phe Asp Phe Glu Asp Lys Leu Phe Ile Lys Gly Leu Val |     |     |
|    | 115   | 120 | 125 |
| 10 | Leu Glu Glu Glu Lys Thr Phe Ala Val Asp His Asp Ala Thr Val Val |     |     |
|    | 130   | 135 | 140 |
|    | Glu Ala Asp Gly Thr Glu Val Arg Ile Ala Pro Leu Asp Val Gln Tyr |     |     |
|    | 145   | 150 | 155 |
| 15 | Gln Asn Ala Thr Ile Trp Gly Lys Leu Ile Thr Asn Phe Ala Gly Pro |     |     |
|    | 165   | 170 | 175 |
|    | Met Asn Asn Phe Ile Leu Gly Val Val Val Phe Trp Val Leu Ile Phe |     |     |
|    | 180   | 185 | 190 |
| 20 | Met Gln Gly Gly Val Arg Asp Val Asp Thr Asn Gln Phe His Ile Met |     |     |
|    | 195   | 200 | 205 |
| 25 | Pro Gln Gly Ala Leu Ala Lys Val Gly Val Pro Glu Thr Ala Gln Ile |     |     |
|    | 210   | 215 | 220 |
|    | Thr Lys Ile Gly Ser His Glu Val Ser Asn Trp Glu Ser Leu Ile Gln |     |     |
|    | 225   | 230 | 235 |
| 30 | Ala Val Glu Thr Glu Thr Lys Asp Lys Thr Ala Pro Thr Leu Asp Val |     |     |
|    | 245   | 250 | 255 |
|    | Thr Ile Ser Glu Lys Gly Ser Asp Lys Gln Val Thr Val Thr Pro Glu |     |     |
|    | 260   | 265 | 270 |
| 35 | Asp Ser Gln Gly Arg Tyr Leu Leu Gly Val Gln Pro Gly Val Lys Ser |     |     |
|    | 275   | 280 | 285 |
| 40 | Asp Phe Leu Ser Met Phe Val Gly Gly Phe Thr Thr Ala Ala Asp Ser |     |     |
|    | 290   | 295 | 300 |
|    | Ala Leu Arg Ile Leu Ser Ala Leu Lys Asn Leu Ile Phe Gln Pro Asp |     |     |
|    | 305   | 310 | 315 |
| 45 | Leu Asn Lys Leu Gly Gly Pro Val Ala Ile Phe Lys Ala Ser Ser Asp |     |     |
|    | 325   | 330 | 335 |
|    | Ala Ala Lys Asn Gly Ile Glu Asn Ile Leu Tyr Phe Leu Ala Met Ile |     |     |
|    | 340   | 345 | 350 |
| 50 | Ser Ile Asn Ile Gly Ile Phe Asn Leu Ile Pro Ile Pro Ala Leu Asp |     |     |
|    | 355   | 360 | 365 |
| 55 | Gly Gly Lys Ile Val Leu Asn Ile Leu Glu Ala Ile Arg Arg Lys Pro |     |     |
|    | 370   | 375 | 380 |
|    | Leu Lys Gln Glu Ile Glu Thr Tyr Val Thr Leu Ala Gly Val Val Ile |     |     |

385                      390                      395                      400  
 Met Val Val Leu Met Ile Ala Val Thr Trp Asn Asp Ile Met Arg Leu  
                                  405                      410                      415  
 5     Phe Phe Arg  
  
 10    <210> 148  
       <211> 197  
       <212> PRT  
       <213> Streptococcus pneumoniae  
  
 15    <400> 148  
 Met Tyr Ala Tyr Leu Lys Gly Ile Ile Thr Lys Ile Thr Ala Lys Tyr  
       1                      5                      10                      15  
 Ile Val Leu Glu Thr Asn Gly Ile Gly Tyr Ile Leu His Val Ala Asn  
 20                      20                      25                      30  
 Pro Tyr Ala Tyr Ser Gly Gln Val Asn Gln Glu Ala Gln Ile Tyr Val  
                     35                      40                      45  
 25    His Gln Val Val Arg Glu Asp Ala His Leu Leu Tyr Gly Phe Arg Ser  
             50                      55                      60  
 Glu Asp Glu Lys Lys Leu Phe Leu Ser Leu Ile Ser Val Ser Gly Ile  
       65                      70                      75                      80  
 30    Gly Pro Val Ser Ala Leu Ala Ile Ile Ala Ala Asp Asp Asn Ala Gly  
                     85                      90                      95  
 Leu Val Gln Ala Ile Glu Thr Lys Asn Ile Thr Tyr Leu Thr Lys Phe  
 35                      100                      105                      110  
 Pro Lys Ile Gly Lys Lys Thr Ala Gln Gln Met Val Leu Asp Leu Glu  
       115                      120                      125  
 40    Gly Lys Val Val Val Ala Gly Asp Asp Leu Pro Ala Lys Val Ala Val  
             130                      135                      140  
 Gln Ala Ser Ala Glu Asn Gln Glu Leu Glu Glu Ala Met Glu Ala Met  
       145                      150                      155                      160  
 45    Leu Ala Leu Gly Tyr Lys Ala Thr Glu Leu Lys Lys Ile Lys Lys Phe  
                     165                      170                      175  
 Phe Glu Gly Thr Thr Asp Thr Ala Glu Asn Tyr Ile Lys Ser Ala Leu  
 50                      180                      185                      190  
 Lys Met Leu Val Lys  
       195  
  
 55    <210> 149  
       <211> 257

&lt;212&gt; PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 149

5 Met Lys Asn Asn Arg Ile Leu Ala Leu Ser Gly Asn Asp Ile Phe Ser  
    1                      5                      10                      15  
  
   Gly Gly Gly Leu Ser Ala Asp Leu Ala Thr Tyr Thr Leu Asn Gly Leu  
           20                      25                      30  
 10 His Gly Phe Val Ala Val Thr Cys Leu Thr Ala Leu Thr Glu Lys Gly  
           35                      40                      45  
  
   Phe Glu Val Phe Pro Thr Asp Asp Thr Ile Phe Gln His Glu Leu Asp  
 15          50                      55                      60  
  
   Ser Leu Arg Asp Val Glu Phe Gly Gly Ile Lys Ile Gly Leu Leu Pro  
    65                      70                      75                      80  
 20 Thr Val Ser Val Ala Glu Lys Ala Leu Asp Phe Ile Lys Gln Arg Pro  
           85                      90                      95  
  
   Gly Val Pro Val Val Leu Asp Pro Val Leu Val Cys Lys Glu Thr His  
           100                      105                      110  
 25 Asp Val Ala Val Ser Glu Leu Cys Gln Glu Leu Ile Arg Phe Phe Pro  
           115                      120                      125  
  
   Tyr Val Ser Val Ile Thr Pro Asn Leu Pro Glu Ala Glu Leu Leu Ser  
 30          130                      135                      140  
  
   Gly Gln Glu Ile Lys Thr Leu Glu Asp Met Lys Thr Ala Ala Gln Lys  
   145                      150                      155                      160  
 35 Leu His Asp Leu Gly Ala Pro Ala Val Ile Ile Lys Gly Gly Asn Arg  
           165                      170                      175  
  
   Leu Ser Gln Asp Lys Ala Val Asp Val Phe Tyr Asp Gly Gln Thr Phe  
           180                      185                      190  
 40 Thr Ile Leu Glu Asn Pro Val Ile Gln Gly Gln Asn Ala Gly Ala Gly  
           195                      200                      205  
  
   Cys Thr Phe Ala Ser Ser Ile Ala Ser His Leu Val Lys Gly Asp Lys  
 45          210                      215                      220  
  
   Phe Leu Pro Ala Val Glu Ser Ser Lys Ala Phe Val Tyr Arg Ala Ile  
   225                      230                      235                      240  
 50 Ala Gln Ala Asp Gln Tyr Gly Val Arg Gln Tyr Glu Ala Asn Lys Asn  
           245                      250                      255

Asn

55

&lt;210&gt; 150

<211> 412  
 <212> PRT  
 <213> Streptococcus pneumoniae

5 <400> 150  
 Met Ile Glu Thr Glu Lys Lys Glu Glu Arg Val Leu Leu Ile Gly Val  
 1 5 10 15  
 Glu Leu Gln Gly Met Asp Ser Phe Asp Leu Ser Met Glu Glu Leu Ala  
 10 20 25 30  
 Ser Leu Ala Lys Thr Ala Gly Ala Val Val Val Asp Ser Tyr Arg Gln  
 35 40 45  
 15 Lys Arg Glu Lys Tyr Asp Ser Lys Thr Phe Val Gly Ser Gly Lys Leu  
 50 55 60  
 Glu Glu Ile Ala Leu Met Val Asp Ala Glu Glu Ile Thr Thr Val Ile  
 65 70 75 80  
 20 Val Asn Asn Arg Leu Thr Pro Arg Gln Asn Val Asn Leu Glu Glu Val  
 85 90 95  
 25 Leu Gly Val Lys Val Ile Asp Arg Met Gln Leu Ile Leu Asp Ile Phe  
 100 105 110  
 Ala Met Arg Ala Arg Ser His Glu Gly Lys Leu Gln Val His Leu Ala  
 115 120 125  
 30 Gln Phe Lys Tyr Leu Leu Pro Arg Leu Val Gly Gln Gly Ile Met Leu  
 130 135 140  
 Ser Arg Gln Ala Gly Gly Ile Gly Ser Arg Gly Pro Gly Glu Ser Gln  
 145 150 155 160  
 35 Leu Glu Leu Asn Arg Arg Ser Val Arg Asn Gln Ile Thr Asp Ile Glu  
 165 170 175  
 Arg Gln Leu Lys Val Val Glu Lys Asn Arg Ala Thr Val Arg Glu Lys  
 180 185 190  
 40 Arg Leu Glu Ser Ser Thr Phe Lys Ile Gly Leu Ile Gly Tyr Thr Asn  
 195 200 205  
 45 Ala Gly Lys Ser Thr Ile Met Asn Ile Leu Thr Ser Lys Thr Gln Tyr  
 210 215 220  
 Glu Ala Asp Glu Leu Phe Ala Thr Leu Asp Ala Thr Thr Lys Ser Ile  
 225 230 235 240  
 50 His Leu Gly Gly Asn Leu Gln Val Thr Leu Thr Asp Thr Val Gly Phe  
 245 250 255  
 Ile Gln Asp Leu Pro Thr Glu Leu Val Ser Ser Phe Lys Ser Thr Leu  
 260 265 270  
 55 Glu Glu Ser Lys His Val Asp Leu Leu Val His Val Ile Asp Ala Ser

275                      280                      285  
 Asn Pro Tyr His Glu Glu His Glu Lys Thr Val Leu Ser Ile Met Lys  
 290                      295                      300  
 5 Asp Leu Asp Met Glu Asp Ile Pro His Leu Thr Leu Tyr Asn Lys Ala  
 305                      310                      315                      320  
 10 Asp Leu Val Glu Asp Phe Thr Pro Thr Gln Thr Pro Tyr Thr Leu Ile  
 325                      330                      335  
 Ser Ala Lys Ser Glu Asp Ser Arg Glu Asn Leu Gln Ala Leu Leu Leu  
 340                      345                      350  
 15 Asp Lys Ile Lys Glu Ile Phe Glu Ala Phe Thr Leu Arg Val Pro Phe  
 355                      360                      365  
 Ser Lys Ser Tyr Lys Ile His Asp Leu Glu Ser Val Ala Ile Leu Glu  
 370                      375                      380  
 20 Glu Arg Asp Tyr Gln Glu Asp Gly Glu Val Ile Thr Gly Tyr Ile Ser  
 385                      390                      395                      400  
 25 Glu Lys Asn Lys Trp Arg Leu Glu Glu Phe Tyr Asp  
 405                      410  
 <210> 151  
 <211> 160  
 30 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 151  
 Met Ala Glu Lys Thr Tyr Pro Met Thr Leu Glu Glu Lys Glu Lys Leu  
 1                      5                      10                      15  
 35 Glu Lys Glu Leu Glu Glu Leu Lys Leu Val Arg Arg Pro Glu Val Val  
 20                      25                      30  
 40 Glu Arg Ile Lys Ile Ala Arg Ser Tyr Gly Asp Leu Ser Glu Asn Ser  
 35                      40                      45  
 Glu Tyr Glu Ala Ala Lys Asp Glu Gln Ala Phe Val Glu Gly Gln Ile  
 50                      55                      60  
 45 Ser Ser Leu Glu Thr Lys Ile Arg Tyr Ala Glu Ile Val Asn Ser Asp  
 65                      70                      75                      80  
 50 Ala Val Ala Gln Asp Glu Val Ala Ile Gly Lys Thr Val Thr Ile Gln  
 85                      90                      95  
 Glu Ile Gly Glu Asp Glu Glu Glu Val Tyr Ile Ile Val Gly Ser Ala  
 100                      105                      110  
 55 Gly Ala Asp Ala Phe Ala Gly Lys Val Ser Asn Glu Ser Pro Ile Gly  
 115                      120                      125

Gln Ala Leu Ile Gly Lys Lys Thr Gly Asp Thr Ala Thr Ile Glu Thr  
 130 135 140

5 Pro Val Gly Ser Tyr Asp Val Lys Ile Leu Lys Val Glu Lys Thr Ala  
 145 150 155 160

10  
 <210> 152  
 <211> 189  
 <212> PRT  
 <213> Streptococcus pneumoniae

15  
 <400> 152  
 Met Thr Lys Leu Leu Val Gly Leu Gly Asn Pro Gly Asp Lys Tyr Phe  
 1 5 10 15

20 Glu Thr Lys His Asn Val Gly Phe Met Leu Ile Asp Gln Leu Ala Lys  
 20 25 30

Lys Gln Asn Val Thr Phe Thr His Asp Lys Ile Phe Gln Ala Asp Leu  
 35 40 45

25 Ala Ser Phe Phe Leu Asn Gly Glu Lys Ile Tyr Leu Val Lys Pro Thr  
 50 55 60

30 Thr Phe Met Asn Glu Ser Gly Lys Ala Val His Ala Leu Leu Thr Tyr  
 65 70 75 80

Tyr Gly Leu Asp Ile Asp Asp Leu Leu Ile Ile Tyr Asp Asp Leu Asp  
 85 90 95

35 Met Glu Val Gly Lys Ile Arg Leu Arg Ala Lys Gly Ser Ala Gly Gly  
 100 105 110

His Asn Gly Ile Lys Ser Ile Ile Gln His Ile Gly Thr Gln Val Phe  
 115 120 125

40 Asn Arg Val Lys Ile Gly Ile Gly Arg Pro Lys Asn Gly Met Ser Val  
 130 135 140

45 Val His His Val Leu Ser Lys Phe Asp Arg Asp Glu Tyr Ile Gly Ile  
 145 150 155 160

Leu Gln Ser Val Asp Lys Val Asp Asp Ser Val Asn Tyr Tyr Leu Gln  
 165 170 175

50 Glu Lys Asn Phe Glu Lys Thr Met Gln Arg Tyr Asn Gly  
 180 185

55  
 <210> 153  
 <211> 283  
 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 153  
 Met Ile Leu Ile Thr Gly Ala Asn Gly Gln Leu Gly Thr Glu Leu Arg  
 1 5 10 15  
 5 Tyr Leu Leu Asp Glu Arg Asn Glu Glu Tyr Val Ala Val Asp Val Ala  
 20 25 30  
 10 Lys Met Asp Ile Thr Asn Glu Glu Met Val Glu Lys Val Phe Glu Glu  
 35 40 45  
 Val Lys Pro Thr Leu Val Tyr His Cys Ala Ala Tyr Thr Ala Val Asp  
 50 55 60  
 15 Ala Ala Glu Asp Glu Gly Lys Glu Leu Asp Phe Ala Ile Asn Val Thr  
 65 70 75 80  
 Gly Thr Lys Asn Val Ala Lys Ala Ser Glu Lys His Gly Ala Thr Leu  
 85 90 95  
 20 Val Tyr Ile Ser Thr Asp Tyr Val Phe Asp Gly Lys Lys Pro Val Gly  
 100 105 110  
 25 Gln Glu Trp Glu Val Asp Asp Arg Pro Asp Pro Gln Thr Glu Tyr Gly  
 115 120 125  
 Arg Thr Lys Arg Met Gly Glu Glu Leu Val Glu Lys His Val Ser Asn  
 130 135 140  
 30 Phe Tyr Ile Ile Arg Thr Ala Trp Val Phe Gly Asn Tyr Gly Lys Asn  
 145 150 155 160  
 Phe Val Phe Thr Met Gln Asn Leu Ala Lys Thr His Lys Thr Leu Thr  
 165 170 175  
 35 Val Val Asn Asp Gln Tyr Gly Arg Pro Thr Trp Thr Arg Thr Leu Ala  
 180 185 190  
 40 Glu Phe Met Thr Tyr Leu Ala Glu Asn Arg Lys Glu Phe Gly Tyr Tyr  
 195 200 205  
 His Leu Ser Asn Asp Ala Thr Glu Asp Thr Thr Trp Tyr Asp Phe Ala  
 210 215 220  
 45 Val Glu Ile Leu Lys Asp Thr Asp Val Glu Val Lys Pro Val Asp Ser  
 225 230 235 240  
 Ser Gln Phe Pro Ala Lys Ala Lys Arg Pro Leu Asn Ser Thr Met Ser  
 245 250 255  
 50 Leu Ala Lys Ala Lys Ala Thr Gly Phe Val Ile Pro Thr Trp Gln Asp  
 260 265 270  
 55 Ala Leu Gln Glu Phe Tyr Lys Gln Glu Val Arg  
 275 280

<210> 154  
 <211> 407  
 5 <212> PRT  
 <213> Streptococcus pneumoniae  
  
 <400> 154  
 10 Met Lys Arg Ser Leu Asp Ser Arg Val Asp Tyr Ser Leu Leu Leu Pro  
     1                    5                    10                    15  
  
     Val Phe Phe Leu Leu Val Ile Gly Val Val Ala Ile Tyr Ile Ala Val  
                     20                    25                    30  
  
 15 Ser His Asp Tyr Pro Asn Asn Ile Leu Pro Ile Leu Gly Gln Gln Val  
                     35                    40                    45  
  
     Ala Trp Ile Ala Leu Gly Leu Val Ile Gly Phe Val Val Met Leu Phe  
                     50                    55                    60  
 20 Asn Thr Glu Phe Leu Trp Lys Val Thr Pro Phe Leu Tyr Ile Leu Gly  
     65                    70                    75                    80  
  
     Leu Gly Leu Met Ile Leu Pro Ile Val Phe Tyr Asn Pro Ser Leu Val  
 25                    85                    90                    95  
  
     Ala Ser Thr Gly Ala Lys Asn Trp Val Ser Ile Asn Gly Ile Thr Leu  
                     100                    105                    110  
  
 30 Phe Gln Pro Ser Glu Phe Met Lys Ile Ser Tyr Ile Leu Met Leu Ala  
                     115                    120                    125  
  
     Arg Val Ile Val Gln Phe Thr Lys Lys His Lys Glu Trp Arg Arg Thr  
                     130                    135                    140  
 35 Val Pro Leu Asp Phe Leu Leu Ile Phe Trp Met Ile Leu Phe Thr Ile  
     145                    150                    155                    160  
  
     Pro Val Leu Val Leu Leu Ala Leu Gln Ser Asp Leu Gly Thr Ala Leu  
 40                    165                    170                    175  
  
     Val Phe Val Ala Ile Phe Ser Gly Ile Val Leu Leu Ser Gly Val Ser  
                     180                    185                    190  
  
 45 Trp Lys Ile Ile Ile Pro Val Phe Val Thr Ala Val Thr Gly Val Ala  
                     195                    200                    205  
  
     Gly Phe Leu Ala Ile Phe Ile Ser Lys Asp Gly Arg Ala Phe Leu His  
                     210                    215                    220  
 50 Gln Ile Gly Met Pro Thr Tyr Gln Ile Asn Arg Ile Leu Ala Trp Leu  
     225                    230                    235                    240  
  
     Asn Pro Phe Glu Phe Ala Gln Thr Thr Thr Tyr Gln Gln Ala Gln Gly  
 55                    245                    250                    255  
  
     Gln Ile Ala Ile Gly Ser Gly Gly Leu Phe Gly Gln Gly Phe Asn Ala



|    | 260   | 265 | 270 |
|----|---|-----|-----|
|    | Ser Asn Leu Leu Ile Pro Val Arg Glu Ser Asp Met Ile Phe Thr Val |     |     |
|    | 275   | 280 | 285 |
| 5  | Ile Ala Glu Asp Phe Gly Phe Ile Gly Ser Val Leu Val Ile Ala Leu |     |     |
|    | 290   | 295 | 300 |
| 10 | Tyr Leu Met Leu Ile Tyr Arg Met Leu Lys Ile Thr Leu Lys Ser Asn |     |     |
|    | 305   | 310 | 315 |
|    | Asn Gln Phe Tyr Thr Tyr Ile Ser Thr Gly Leu Ile Met Met Leu Leu |     |     |
|    | 325   | 330 | 335 |
| 15 | Phe His Ile Phe Glu Asn Ile Gly Ala Val Thr Gly Leu Leu Pro Leu |     |     |
|    | 340   | 345 | 350 |
|    | Thr Gly Ile Pro Leu Pro Phe Ile Ser Gln Gly Gly Ser Ala Ile Ile |     |     |
|    | 355   | 360 | 365 |
| 20 | Ser Asn Leu Ile Gly Val Gly Leu Leu Leu Ser Met Ser Tyr Gln Thr |     |     |
|    | 370   | 375 | 380 |
| 25 | Asn Leu Ala Glu Glu Lys Ser Gly Lys Val Pro Phe Lys Arg Lys Lys |     |     |
|    | 385   | 390 | 395 |
|    | Val Val Leu Lys Gln Ile Lys                                     |     |     |
|    | 405   |     |     |
| 30 | <210> 155   |     |     |
|    | <211> 202   |     |     |
|    | <212> PRT   |     |     |
|    | <213> Streptococcus pneumoniae                                  |     |     |
| 35 | <400> 155   |     |     |
|    | Met Gly Lys Ile Ile Gly Ile Thr Gly Gly Ile Ala Ser Gly Lys Ser |     |     |
|    | 1 5 10 15   |     |     |
| 40 | Thr Val Thr Asn Phe Leu Lys His Gln Gly Leu Ser Ser Ser Gly Leu |     |     |
|    | 20 25 30  |     |     |
|    | Pro Thr Gln Cys Ser Thr Asn Tyr Arg Lys Pro Gly Gly Arg Leu Phe |     |     |
|    | 35 40 45  |     |     |
| 45 | Glu Ala Leu Val Gln His Phe Gly Gln Glu Ile Ile Leu Glu Asn Gly |     |     |
|    | 50 55 60  |     |     |
|    | Glu Leu Asn Arg Pro Leu Ile Ala Ser Leu Ile Phe Ser Asn Pro Glu |     |     |
| 50 | 65 70 75 80   |     |     |
|    | Glu Gln Lys Trp Ser Asn Gln Ile Gln Gly Glu Ile Ile Arg Glu Glu |     |     |
|    | 85 90 95  |     |     |
| 55 | Leu Ala Thr Leu Arg Glu Gln Leu Ala Gln Thr Glu Glu Ile Phe Phe |     |     |
|    | 100 105 110   |     |     |

Met Asp Ile Pro Leu Leu Phe Glu Gln Asp Tyr Ser Asp Trp Phe Ala  
 115 120 125  
 5 Glu Thr Trp Leu Val Tyr Val Asp Arg Asp Ala Gln Val Glu Arg Leu  
 130 135 140  
 Met Lys Arg Asp Gln Leu Ser Lys Asp Glu Ala Glu Ser Arg Met Ala  
 145 150 155 160  
 10 Ala Gln Trp Pro Leu Glu Lys Lys Lys Asp Leu Ala Ser Gln Val Leu  
 165 170 175  
 Asp Asn Asn Gly Asn Gln Asn Gln Leu Leu Asn Gln Val His Ile Leu  
 180 185 190  
 15 Leu Glu Gly Gly Arg Gln Asp Asp Arg Asp  
 195 200  
 20 <210> 156  
 <211> 419  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 25 <400> 156  
 Met Arg Lys Ile Val Ile Asn Gly Gly Leu Pro Leu Gln Gly Glu Ile  
 1 5 10 15  
 30 Thr Ile Ser Gly Ala Lys Asn Ser Val Val Ala Leu Ile Pro Ala Ile  
 20 25 30  
 Ile Leu Ala Asp Asp Val Val Thr Leu Asp Cys Val Pro Asp Ile Ser  
 35 40 45  
 35 Asp Val Ala Ser Leu Val Glu Ile Met Glu Leu Met Gly Ala Thr Val  
 50 55 60  
 Lys Arg Tyr Asp Asp Val Leu Glu Ile Asp Pro Arg Gly Val Gln Asn  
 65 70 75 80  
 40 Ile Pro Met Pro Tyr Gly Lys Ile Asn Ser Leu Arg Ala Ser Tyr Tyr  
 85 90 95  
 Phe Tyr Gly Ser Leu Leu Gly Arg Phe Gly Glu Ala Thr Val Gly Leu  
 100 105 110  
 45 Pro Gly Gly Cys Asp Leu Gly Pro Arg Pro Ile Asp Leu His Leu Lys  
 115 120 125  
 50 Ala Phe Glu Ala Met Gly Ala Thr Ala Ser Tyr Glu Gly Asp Asn Met  
 130 135 140  
 Lys Leu Ser Ala Lys Asp Thr Gly Leu His Gly Ala Ser Ile Tyr Met  
 145 150 155 160  
 55 Asp Thr Val Ser Val Gly Ala Thr Ile Asn Thr Met Ile Ala Ala Val  
 165 170 175

Lys Ala Asn Gly Arg Thr Ile Ile Glu Asn Ala Ala Arg Glu Pro Glu  
                     180                    185                    190  
 5 Ile Ile Asp Val Ala Thr Leu Leu Asn Asn Met Gly Ala His Ile Arg  
                     195                    200                    205  
 Gly Ala Gly Thr Asn Ile Ile Ile Ile Asp Gly Val Glu Arg Leu His  
                     210                    215                    220  
 10 Gly Thr Arg His Gln Val Ile Pro Asp Arg Ile Glu Ala Gly Thr Tyr  
                     225                    230                    235                    240  
 15 Ile Ser Leu Ala Ala Ala Val Gly Lys Gly Ile Arg Ile Asn Asn Val  
                     245                    250                    255  
 Leu Tyr Glu His Leu Glu Gly Phe Ile Ala Lys Leu Glu Glu Met Gly  
                     260                    265                    270  
 20 Val Arg Met Thr Val Ser Glu Asp Ser Ile Phe Val Glu Glu Gln Ser  
                     275                    280                    285  
 Asn Leu Lys Ala Ile Asn Ile Lys Thr Ala Pro Tyr Pro Gly Phe Ala  
                     290                    295                    300  
 25 Thr Asp Leu Gln Gln Pro Leu Thr Pro Leu Leu Leu Arg Ala Asn Gly  
                     305                    310                    315                    320  
 30 Arg Gly Thr Ile Val Asp Thr Ile Tyr Glu Lys Arg Val Asn His Val  
                     325                    330                    335  
 Phe Glu Leu Ala Lys Met Asp Ala Asp Ile Ser Thr Thr Asn Gly His  
                     340                    345                    350  
 35 Ile Leu Tyr Thr Gly Gly Arg Asp Leu Arg Gly Ala Ser Val Lys Ala  
                     355                    360                    365  
 Thr Asp Leu Arg Ala Gly Ala Ala Leu Val Ile Ala Gly Leu Met Ala  
                     370                    375                    380  
 40 Glu Gly Lys Thr Glu Ile Thr Asn Ile Glu Phe Ile Leu Arg Gly Tyr  
                     385                    390                    395                    400  
 45 Ser Asp Ile Ile Glu Lys Leu Arg Asn Leu Gly Ala Asp Ile Arg Leu  
                     405                    410                    415  
 Val Glu Asp  
 50  
 <210> 157  
 <211> 231  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 55  
 <400> 157  
 Met Ser Arg Ile Glu Phe Ser Pro Ser Leu Met Thr Met Asp Leu Asp

98

Ala Asn Tyr Pro Phe Ala Thr Ile Asp Pro Asn Val Gly Met Val Glu  
                   35                                  40                                  45  
 5 Asp Pro Asp Glu Arg Leu Gln Lys Leu Thr Glu Met Ile Thr Pro Lys  
           50                                  55                                  60  
 Lys Thr Val Pro Thr Thr Phe Glu Phe Thr Asp Ile Ala Gly Ile Val  
   65                                  70                                  75                                  80  
 10 Lys Gly Ala Ser Lys Gly Glu Gly Leu Gly Asn Lys Phe Leu Ala Asn  
                   85                                  90                                  95  
 Ile Arg Glu Val Asp Ala Ile Val His Val Val Arg Ala Phe Asp Asp  
                   100                                  105                                  110  
 15 Glu Asn Val Met Arg Glu Gln Gly Arg Glu Asp Ala Phe Val Asp Pro  
                   115                                  120                                  125  
 20 Leu Ala Asp Ile Asp Thr Ile Asn Leu Glu Leu Ile Leu Ala Asp Leu  
           130                                  135                                  140  
 Glu Ser Val Asn Lys Arg Tyr Ala Arg Val Glu Lys Met Ala Arg Thr  
   145                                  150                                  155                                  160  
 25 Gln Lys Asp Lys Glu Ser Val Ala Glu Phe Asn Val Leu Gln Lys Ile  
                   165                                  170                                  175  
 Lys Pro Val Leu Glu Asp Gly Lys Ser Ala Arg Thr Ile Glu Phe Thr  
                   180                                  185                                  190  
 30 Asp Glu Glu Gln Lys Val Val Lys Gly Leu Phe Leu Leu Thr Thr Lys  
           195                                  200                                  205  
 35 Pro Val Leu Tyr Val Ala Asn Val Asp Glu Asp Val Val Ser Glu Pro  
           210                                  215                                  220  
 Asp Ser Ile Asp Tyr Val Lys Gln Ile Arg Glu Phe Ala Ala Thr Glu  
   225                                  230                                  235                                  240  
 40 Asn Ala Glu Val Val Val Ile Ser Ala Arg Ala Glu Glu Glu Ile Ser  
                   245                                  250                                  255  
 Glu Leu Asp Asp Glu Asp Lys Lys Glu Phe Leu Glu Ala Ile Gly Leu  
                   260                                  265                                  270  
 45 Thr Glu Ser Gly Val Asp Lys Leu Thr Arg Ala Ala Tyr His Leu Leu  
           275                                  280                                  285  
 50 Gly Leu Gly Thr Tyr Phe Thr Ala Gly Glu Lys Glu Val Arg Ala Trp  
           290                                  295                                  300  
 Thr Phe Lys Arg Gly Met Lys Ala Pro Gln Ala Ala Gly Ile Ile His  
   305                                  310                                  315                                  320  
 55 Ser Asp Phe Glu Lys Gly Phe Ile Arg Ala Val Thr Met Ser Tyr Glu  
                   325                                  330                                  335

Asp Leu Val Lys Tyr Gly Ser Glu Lys Ala Val Lys Glu Ala Gly Arg  
                   340                                  345                                  350  
 5 Leu Arg Glu Glu Gly Lys Glu Tyr Ile Val Gln Asp Gly Asp Ile Met  
                   355                                  360                                  365  
 Glu Phe Arg Phe Asn Val  
                   370  
 10 <210> 159  
     <211> 110  
     <212> PRT  
     <213> Streptococcus pneumoniae  
 15 <400> 159  
 Met Glu Ile Glu Lys Thr Asn Arg Met Asn Ala Leu Phe Glu Phe Tyr  
     1                                  5                                  10                                  15  
 20 Ala Ala Leu Leu Thr Asp Lys Gln Met Asn Tyr Ile Glu Leu Tyr Tyr  
                   20                                  25                                  30  
 Ala Asp Asp Tyr Ser Leu Ala Glu Ile Ala Glu Glu Phe Gly Val Ser  
                   35                                  40                                  45  
 25 Arg Gln Ala Val Tyr Asp Asn Ile Lys Arg Thr Glu Lys Ile Leu Glu  
                   50                                  55                                  60  
 30 Asp Tyr Glu Met Lys Leu His Met Tyr Ser Asp Tyr Ile Val Arg Ser  
                   65                                  70                                  75                                  80  
 Gln Ile Phe Asp Gln Ile Leu Glu Arg Tyr Pro Lys Asp Asp Phe Leu  
                                   85                                  90                                  95  
 35 Gln Glu Gln Ile Glu Ile Leu Thr Ser Ile Asp Asn Arg Glu  
                   100                                  105                                  110  
 40 <210> 160  
     <211> 223  
     <212> PRT  
     <213> Streptococcus pneumoniae  
 45 <400> 160  
 Met Thr Leu Glu Trp Glu Glu Phe Leu Asp Pro Tyr Ile Gln Ala Val  
     1                                  5                                  10                                  15  
 Gly Glu Leu Lys Ile Lys Leu Arg Gly Ile Arg Lys Gln Tyr Arg Lys  
                   20                                  25                                  30  
 50 Gln Asn Lys His Ser Pro Ile Glu Phe Val Thr Gly Arg Val Lys Pro  
                   35                                  40                                  45  
 55 Ile Glu Ser Ile Lys Glu Lys Met Ala Arg Arg Gly Ile Thr Tyr Ala  
                   50                                  55                                  60  
 Thr Leu Glu His Asp Leu Gln Asp Ile Ala Gly Leu Arg Val Met Val

101

Ser Leu Val Asp Leu Arg His Asp Pro Ser Ala Asp Asp Val Gln Met  
 115 120 125  
 Tyr Glu Phe Leu Lys Tyr Tyr Glu Ile Pro Val Ile Ile Val Ala Thr  
 5 130 135 140  
 Lys Ala Asp Lys Ile Pro Arg Gly Lys Trp Asn Lys His Glu Ser Ala  
 145 150 155 160  
 10 Ile Lys Lys Lys Leu Asn Phe Asp Pro Ser Asp Asp Phe Ile Leu Phe  
 165 170 175  
 Ser Ser Val Ser Lys Ala Gly Met Asp Glu Ala Trp Asp Ala Ile Leu  
 180 185 190  
 15 Glu Lys Leu  
 195  
 20 <210> 162  
 <211> 97  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 25 <400> 162  
 Met Lys Thr Arg Lys Ile Pro Leu Arg Lys Ser Val Val Ser Asn Glu  
 1 5 10 15  
 Val Ile Asp Lys Arg Asp Leu Leu Arg Ile Val Lys Asn Lys Glu Gly  
 30 20 25 30  
 Gln Val Phe Ile Asp Pro Thr Gly Lys Ala Asn Gly Arg Gly Ala Tyr  
 35 40 45  
 35 Ile Lys Leu Asp Asn Ala Glu Ala Leu Glu Ala Lys Lys Lys Val  
 50 55 60  
 Phe Asn Arg Ser Phe Ser Met Glu Val Glu Glu Ser Phe Tyr Asp Glu  
 65 70 75 80  
 40 Leu Ile Ala Tyr Val Asp His Lys Val Lys Arg Arg Glu Leu Gly Leu  
 85 90 95  
 Glu  
 45  
 50 <210> 163  
 <211> 103  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 163  
 Met Leu Lys Pro Ser Ile Asp Thr Leu Leu Asp Lys Val Pro Ser Lys  
 55 1 5 10 15  
 Tyr Ser Leu Val Ile Leu Glu Ala Lys Arg Ala His Glu Leu Glu Ala



20 25 30  
 Gly Ala Pro Ala Thr Gln Gly Phe Lys Ser Glu Lys Ser Thr Leu Arg  
 35 40 45  
 5 Ala Leu Glu Glu Ile Glu Ser Gly Asn Val Thr Ile His Pro Asp Pro  
 50 55 60  
 10 Glu Gly Lys Arg Glu Ala Val Arg Arg Arg Ile Glu Glu Glu Lys Arg  
 65 70 75 80  
 Arg Lys Glu Glu Glu Glu Lys Lys Ile Lys Glu Gln Ile Ala Lys Glu  
 85 90 95  
 15 Lys Glu Asp Gly Glu Lys Ile  
 100  
 <210> 164  
 20 <211> 103  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 164  
 25 Met Ser Leu Thr Ser Lys Gln Arg Ala Phe Leu Asn Ser Gln Ala His  
 1 5 10 15  
 Thr Leu Lys Pro Ile Ile Gln Ile Gly Lys Asn Gly Leu Asn Asp Gln  
 20 25 30  
 30 Ile Lys Thr Ser Val Arg Gln Ala Leu Asp Ala Arg Glu Leu Ile Lys  
 35 40 45  
 Val Thr Leu Leu Gln Asn Thr Asp Glu Asn Ile His Glu Val Ala Glu  
 50 55 60  
 35 Ile Leu Glu Glu Glu Ile Gly Val Asp Thr Val Gln Lys Ile Gly Arg  
 65 70 75 80  
 40 Ile Leu Ile Leu Phe Lys Gln Ser Ser Lys Lys Glu Asn Arg Lys Ile  
 85 90 95  
 Ser Lys Lys Val Lys Glu Ile  
 100  
 45  
 <210> 165  
 <211> 175  
 <212> PRT  
 50 <213> Streptococcus pneumoniae  
 <400> 165  
 Met Ala Ile Glu Asn Tyr Ile Pro Asp Phe Ala Val Glu Ala Val Tyr  
 1 5 10 15  
 55 Asp Leu Thr Val Pro Ser Leu Gln Ala Gln Gly Ile Lys Ala Val Leu  
 20 25 30

Val Asp Leu Asp Asn Thr Leu Ile Ala Trp Asn Asn Pro Asp Gly Thr  
 35 40 45  
 5 Pro Glu Met Lys Gln Trp Leu His Asp Leu Arg Asp Ala Gly Ile Gly  
 50 55 60  
 Ile Ile Val Val Ser Asn Asn Thr Lys Lys Arg Val Gln Arg Ala Val  
 65 70 75 80  
 10 Glu Lys Phe Gly Ile Asp Tyr Val Tyr Trp Ala Leu Lys Pro Phe Thr  
 85 90 95  
 Phe Gly Ile Asp Arg Ala Met Lys Glu Phe His Tyr Asp Lys Lys Glu  
 100 105 110  
 15 Val Val Met Val Gly Asp Gln Leu Met Thr Asp Ile Arg Ala Ala His  
 115 120 125  
 20 Arg Ala Gly Ile Arg Ser Ile Leu Val Lys Pro Leu Val Gln His Asp  
 130 135 140  
 Ser Ile Lys Thr Gln Ile Asn Arg Thr Arg Glu Arg Arg Val Met Arg  
 145 150 155 160  
 25 Lys Ile Thr Glu Lys Tyr Gly Pro Ile Thr Tyr Lys Lys Gly Ile  
 165 170 175  
 30 <210> 166  
 <211> 455  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 35 <400> 166  
 Met Phe Arg Lys Ile Leu Ile Ala Asn Arg Gly Glu Ile Ala Val Arg  
 1 5 10 15  
 40 Ile Ile Arg Ala Ala Arg Glu Leu Gly Ile Ala Thr Val Ala Val Tyr  
 20 25 30  
 Ser Thr Ala Asp Lys Glu Ala Leu His Thr Leu Leu Ala Asp Glu Ala  
 35 40 45  
 45 Val Cys Ile Gly Pro Gly Lys Ala Thr Glu Ser Tyr Leu Asn Ile Asn  
 50 55 60  
 Ala Val Leu Ser Ala Ala Val Leu Thr Glu Ala Glu Ala Ile His Pro  
 65 70 75 80  
 50 Gly Phe Gly Phe Leu Ser Glu Asn Ser Lys Phe Ala Thr Met Cys Glu  
 85 90 95  
 Glu Ile Gly Ile Lys Phe Ile Gly Pro Ser Gly His Val Met Asp Met  
 100 105 110  
 55 Met Gly Asp Lys Ile Asn Ala Arg Ala Gln Met Ile Lys Ala Gly Val

|    | 115   | 120     | 125     |
|----|---|---------|---------|
|    | Pro Val Ile Pro Gly Ser Asp Gly Glu Val His Asn Ser Glu Glu Ala |         |         |
|    | 130   | 135     | 140     |
| 5  | Leu Ile Val Ala Glu Lys Ile Gly Tyr Pro Val Met Leu Lys Ala Ser |         |         |
|    | 145   | 150     | 155 160 |
| 10 | Ala Gly Gly Gly Gly Lys Gly Ile Arg Lys Val Glu Lys Pro Asp Asp |         |         |
|    |   | 165 170 | 175     |
|    | Leu Val Ser Ala Phe Glu Thr Ala Ser Ser Glu Ala Lys Ala Asn Tyr |         |         |
|    |   | 180 185 | 190     |
| 15 | Gly Asn Gly Ala Met Tyr Ile Glu Arg Val Ile Tyr Pro Ala Arg His |         |         |
|    |   | 195 200 | 205     |
|    | Ile Glu Val Gln Ile Leu Gly Asp Glu His Gly His Val Ile His Leu |         |         |
|    | 210   | 215     | 220     |
| 20 | Gly Glu Arg Asp Cys Ser Leu Gln Arg Asn Asn Gln Lys Val Leu Glu |         |         |
|    | 225   | 230 235 | 240     |
|    | Glu Ser Pro Ser Ile Ala Ile Gly Lys Thr Leu Arg His Glu Ile Gly |         |         |
| 25 |   | 245 250 | 255     |
|    | Ala Ala Ala Val Arg Ala Ala Glu Phe Val Gly Tyr Glu Asn Ala Gly |         |         |
|    |   | 260 265 | 270     |
| 30 | Thr Ile Glu Phe Leu Leu Asp Glu Ala Ser Ser Asn Phe Tyr Phe Met |         |         |
|    |   | 275 280 | 285     |
|    | Glu Met Asn Thr Arg Val Gln Val Glu His Pro Val Thr Glu Phe Val |         |         |
|    | 290   | 295 300 |         |
| 35 | Ser Gly Val Asp Ile Val Lys Glu Gln Ile Cys Ile Ala Ala Gly Gln |         |         |
|    | 305   | 310 315 | 320     |
|    | Pro Leu Ser Val Lys Gln Glu Asp Ile Val Leu Arg Gly His Ala Ile |         |         |
| 40 |   | 325 330 | 335     |
|    | Glu Cys Arg Ile Asn Ala Glu Asn Pro Ala Phe Asn Phe Ala Pro Ser |         |         |
|    |   | 340 345 | 350     |
| 45 | Pro Gly Lys Ile Thr Asn Leu Tyr Leu Pro Ser Gly Gly Val Gly Leu |         |         |
|    |   | 355 360 | 365     |
|    | Arg Val Asp Ser Ala Val Tyr Pro Gly Tyr Thr Ile Pro Pro Tyr Tyr |         |         |
|    | 370   | 375 380 |         |
| 50 | Asp Ser Met Ile Ala Lys Ile Ile Val His Gly Glu Asn Arg Phe Asp |         |         |
|    | 385   | 390 395 | 400     |
|    | Ala Leu Met Lys Met Gln Arg Ala Leu Tyr Glu Leu Glu Ile Glu Gly |         |         |
| 55 |   | 405 410 | 415     |
|    | Val Gln Thr Asn Ala Asp Phe Gln Leu Asp Leu Ile Ser Asp Arg Asn |         |         |

420                      425                      430  
 Val Ile Ala Gly Asp Tyr Asp Thr Cys Phe Leu Met Glu Thr Phe Leu  
                     435                      440                      445  
 5    Pro Lys Tyr Gln Glu Lys Glu  
                     450                      455  
  
 10   <210> 167  
      <211> 77  
      <212> PRT  
      <213> Streptococcus pneumoniae  
  
 15   <400> 167  
      Met Ile Tyr Lys Val Phe Tyr Gln Glu Thr Lys Glu Arg Ser Pro Arg  
                     1                      5                      10                      15  
 20   Arg Glu Thr Thr Arg Ala Leu Tyr Leu Asp Ile Asp Thr Ser Ser Glu  
                     20                      25                      30  
      Leu Glu Gly Arg Ile Thr Ala Arg Gln Leu Val Glu Glu Asn Arg Pro  
                     35                      40                      45  
 25   Glu Tyr Asn Ile Glu Tyr Ile Glu Leu Leu Ser Asp Lys Leu Leu Asp  
                     50                      55                      60  
      Tyr Glu Lys Glu Thr Gly Ala Phe Glu Ile Thr Glu Phe  
                     65                      70                      75  
 30  
      <210> 168  
      <211> 336  
      <212> PRT  
 35   <213> Streptococcus pneumoniae  
  
      <400> 168  
      Met Lys Asp Arg Tyr Ile Leu Ala Phe Glu Thr Ser Cys Asp Glu Thr  
                     1                      5                      10                      15  
 40   Ser Val Ala Val Leu Lys Asn Asp Asp Glu Leu Leu Ser Asn Val Ile  
                     20                      25                      30  
      Ala Ser Gln Ile Glu Ser His Lys Arg Phe Gly Gly Val Val Pro Glu  
                     35                      40                      45  
      Val Ala Ser Arg His His Val Glu Val Ile Thr Ala Cys Ile Glu Glu  
                     50                      55                      60  
 50   Ala Leu Ala Glu Ala Gly Ile Thr Glu Glu Asp Val Thr Ala Val Ala  
                     65                      70                      75                      80  
      Val Thr Tyr Gly Pro Gly Leu Val Gly Ala Leu Leu Val Gly Leu Ser  
                     85                      90                      95  
 55   Ala Ala Lys Ala Phe Ala Trp Ala His Gly Leu Pro Leu Ile Pro Val  
                     100                      105                      110

Asn His Met Ala Gly His Leu Met Ala Ala Gln Ser Val Glu Pro Leu  
 115 120 125  
 5 Glu Phe Pro Leu Leu Ala Leu Leu Val Ser Gly Gly His Thr Glu Leu  
 130 135 140  
 Val Tyr Val Ser Glu Ala Gly Asp Tyr Lys Ile Val Gly Glu Thr Arg  
 145 150 155 160  
 10 Asp Asp Ala Val Gly Glu Ala Tyr Asp Lys Val Gly Arg Val Met Gly  
 165 170 175  
 Leu Thr Tyr Pro Ala Gly Arg Glu Ile Asp Glu Leu Ala His Gln Gly  
 15 180 185 190  
 Gln Asp Ile Tyr Asp Phe Pro Arg Ala Met Ile Lys Glu Asp Asn Leu  
 195 200 205  
 20 Glu Phe Ser Phe Ser Gly Leu Lys Ser Ala Phe Ile Asn Leu His His  
 210 215 220  
 Asn Ala Glu Gln Lys Gly Glu Ser Leu Ser Thr Glu Asp Leu Cys Ala  
 225 230 235 240  
 25 Ser Phe Gln Ala Ala Val Met Asp Ile Leu Met Ala Lys Thr Lys Lys  
 245 250 255  
 Ala Leu Glu Glu Tyr Pro Val Lys Thr Leu Phe Val Ala Gly Gly Val  
 30 260 265 270  
 Ala Ala Asn Lys Gly Leu Arg Glu Arg Leu Ala Ala Glu Ile Thr Asp  
 275 280 285  
 35 Val Lys Val Ile Ile Pro Pro Leu Arg Leu Cys Gly Asp Asn Ala Gly  
 290 295 300  
 Met Ile Ala Tyr Ala Ser Val Ser Glu Trp Asn Lys Glu Asn Phe Ala  
 305 310 315 320  
 40 Gly Trp Asp Leu Asn Ala Lys Pro Ser Leu Ala Phe Asp Thr Met Glu  
 325 330 335  
 45  
 <210> 169  
 <211> 602  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 169  
 Met Cys Gly Ile Val Gly Val Val Gly Asn Thr Asn Ala Thr Asp Ile  
 55 1 5 10 15  
 Leu Ile Gln Gly Leu Glu Lys Leu Glu Tyr Arg Gly Tyr Asp Ser Ala

|    | 20  | 25  | 30      |
|----|---|-----|---------|
|    | Gly Ile Phe Val Leu Asp Gly Ala Asp Asn His Leu Val Lys Ala Val |     |         |
|    | 35  | 40  | 45      |
| 5  | Gly Arg Ile Ala Glu Leu Ser Ala Lys Thr Ala Gly Val Glu Gly Thr |     |         |
|    | 50  | 55  | 60      |
|    | Thr Gly Ile Gly His Thr Arg Trp Ala Thr His Gly Lys Pro Thr Glu |     |         |
| 10 | 65  | 70  | 75 80   |
|    | Asp Asn Ala His Pro His Arg Ser Glu Thr Glu Arg Phe Val Leu Val |     |         |
|    | 85  | 90  | 95      |
| 15 | His Asn Gly Val Ile Glu Asn Tyr Leu Glu Ile Lys Glu Glu Tyr Leu |     |         |
|    | 100   | 105 | 110     |
|    | Ala Gly His His Phe Lys Gly Gln Thr Asp Thr Glu Ile Ala Val His |     |         |
|    | 115   | 120 | 125     |
| 20 | Leu Ile Gly Lys Phe Ala Glu Glu Glu Gly Leu Ser Val Leu Glu Ala |     |         |
|    | 130   | 135 | 140     |
|    | Phe Lys Lys Ala Leu His Ile Ile Arg Gly Ser Tyr Ala Phe Ala Leu |     |         |
| 25 | 145   | 150 | 155 160 |
|    | Ile Asp Ser Glu Asn Pro Asp Val Ile Tyr Val Ala Lys Asn Lys Ser |     |         |
|    | 165   | 170 | 175     |
| 30 | Pro Leu Leu Ile Gly Leu Gly Glu Gly Tyr Asn Met Val Cys Ser Asp |     |         |
|    | 180   | 185 | 190     |
|    | Ala Met Ala Met Ile Arg Glu Thr Asn Gln Tyr Met Glu Ile His Asp |     |         |
|    | 195   | 200 | 205     |
| 35 | Gln Glu Leu Val Ile Val Lys Ala Asp Ser Val Glu Val Gln Asp Tyr |     |         |
|    | 210   | 215 | 220     |
|    | Asp Gly Asn Ser Arg Glu Arg Ala Ser Tyr Thr Ala Glu Leu Asp Leu |     |         |
| 40 | 225   | 230 | 235 240 |
|    | Ser Asp Ile Gly Lys Gly Thr Tyr Pro Tyr Tyr Met Leu Lys Glu Ile |     |         |
|    | 245   | 250 | 255     |
| 45 | Asp Glu Gln Pro Thr Val Met Arg Lys Leu Ile Gln Ala Tyr Thr Asp |     |         |
|    | 260   | 265 | 270     |
|    | Asp Ala Gly Gln Val Val Val Ala Pro Ala Ile Ile Lys Ala Val Gln |     |         |
|    | 275   | 280 | 285     |
| 50 | Asp Ala Asp Arg Ile Tyr Ile Leu Ala Ala Gly Thr Ser Tyr His Ala |     |         |
|    | 290   | 295 | 300     |
|    | Gly Phe Ala Ser Lys Lys Met Leu Glu Glu Leu Thr Asp Thr Pro Val |     |         |
| 55 | 305   | 310 | 315 320 |
|    | Glu Leu Gly Ile Ser Ser Glu Trp Gly Tyr Gly Met Pro Leu Leu Ser |     |         |

|    |       |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|----|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
|    |       |     |     |     | 325 |     |     |     |     |     | 330 |     |     |     |     | 335 |
|    | Lys   | Lys | Pro | Leu | Phe | Ile | Phe | Ile | Ser | Gln | Ser | Gly | Glu | Thr | Ala | Asp |
|    |       |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |
| 5  | Ser   | Arg | Gln | Val | Leu | Val | Lys | Ala | Asn | Glu | Met | Gly | Ile | Pro | Ser | Leu |
|    |       |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |     |     |     |
| 10 | Thr   | Val | Thr | Asn | Val | Pro | Gly | Ser | Thr | Leu | Ser | Arg | Glu | Ala | Asn | Tyr |
|    |       | 370 |     |     |     |     | 375 |     |     |     |     |     | 380 |     |     |     |
|    | Thr   | Met | Leu | Leu | His | Ala | Gly | Pro | Glu | Ile | Ala | Val | Ala | Ser | Thr | Lys |
|    | 385   |     |     |     |     | 390 |     |     |     |     | 395 |     |     |     |     | 400 |
| 15 | Ala   | Tyr | Thr | Ala | Gln | Ile | Ala | Ala | Leu | Ala | Phe | Leu | Ala | Lys | Ala | Val |
|    |       |     |     |     | 405 |     |     |     |     | 410 |     |     |     |     |     | 415 |
|    | Gly   | Glu | Ala | Asn | Gly | Asn | Ala | Lys | Ala | Gln | Ala | Phe | Asp | Leu | Val | His |
|    |       |     |     | 420 |     |     |     |     | 425 |     |     |     |     | 430 |     |     |
| 20 | Glu   | Leu | Ser | Ile | Val | Ala | Gln | Ser | Ile | Glu | Ser | Thr | Leu | Ser | Glu | Lys |
|    |       |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |     |     |     |
| 25 | Glu   | Thr | Ile | Glu | Ala | Lys | Val | Arg | Glu | Leu | Leu | Glu | Thr | Thr | Arg | Asn |
|    | 450   |     |     |     |     |     | 455 |     |     |     |     |     | 460 |     |     |     |
|    | Ala   | Phe | Tyr | Ile | Gly | Arg | Gly | Gln | Asp | Tyr | Tyr | Val | Ala | Met | Glu | Ala |
|    | 465   |     |     |     |     | 470 |     |     |     |     | 475 |     |     |     |     | 480 |
| 30 | Ser   | Leu | Lys | Leu | Lys | Glu | Ile | Ser | Tyr | Ile | Gln | Cys | Glu | Gly | Phe | Ala |
|    |       |     |     |     | 485 |     |     |     |     | 490 |     |     |     |     | 495 |     |
|    | Ala   | Gly | Glu | Leu | Lys | His | Gly | Thr | Ile | Ala | Leu | Ile | Glu | Glu | Gly | Thr |
|    |       |     |     | 500 |     |     |     |     | 505 |     |     |     |     | 510 |     |     |
| 35 | Pro   | Val | Leu | Ala | Leu | Leu | Ser | Asp | Pro | Val | Leu | Ala | Asn | His | Thr | Arg |
|    |       |     | 515 |     |     |     |     | 520 |     |     |     |     | 525 |     |     |     |
| 40 | Gly   | Asn | Ile | Gln | Glu | Val | Ala | Ala | Arg | Gly | Ala | Lys | Val | Leu | Thr | Ile |
|    | 530   |     |     |     |     |     | 535 |     |     |     |     | 540 |     |     |     |     |
|    | Ala   | Glu | Glu | Asn | Val | Ala | Lys | Asp | Thr | Asp | Asp | Ile | Val | Leu | Thr | Thr |
|    | 545   |     |     |     |     | 550 |     |     |     | 555 |     |     |     |     |     | 560 |
| 45 | Val   | His | Pro | Tyr | Leu | Ser | Pro | Ile | Ser | Met | Val | Val | Pro | Thr | Gln | Leu |
|    |       |     |     |     | 565 |     |     |     |     | 570 |     |     |     |     | 575 |     |
|    | Val   | Ala | Tyr | Phe | Ala | Thr | Leu | His | Arg | Gly | Leu | Asp | Val | Asp | Lys | Pro |
|    |       |     |     | 580 |     |     |     |     | 585 |     |     |     |     | 590 |     |     |
| 50 | Arg   | Asn | Leu | Ala | Lys | Ser | Val | Thr | Val | Glu |     |     |     |     |     |     |
|    |       |     | 595 |     |     |     |     | 600 |     |     |     |     |     |     |     |     |
| 55 | <210> | 170 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <211> | 240 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|    | <212> | PRT |     |     |     |     |     |     |     |     |     |     |     |     |     |     |

<213> Streptococcus pneumoniae

<400> 170

5 Met Ile Arg Ile Glu Asn Leu Ser Val Ser Tyr Lys Glu Thr Leu Ala  
1 5 10 15

Leu Lys Asp Ile Ser Leu Val Leu His Gly Pro Thr Ile Thr Gly Ile  
20 25 30

10 Ile Gly Pro Asn Gly Ala Gly Lys Ser Thr Leu Leu Lys Gly Met Leu  
35 40 45

Gly Ile Ile Pro His Gln Gly Gln Ala Phe Leu Asp Asp Lys Glu Val  
50 55 60

15 Lys Lys Ser Leu His Arg Ile Ala Tyr Val Glu Gln Lys Ile Asn Ile  
65 70 75 80

20 Asp Tyr Asn Phe Pro Ile Lys Val Lys Glu Cys Val Ser Leu Gly Leu  
85 90 95

Phe Pro Ser Ile Pro Leu Phe Arg Ser Leu Lys Ala Lys His Trp Lys  
100 105 110

25 Lys Val Gln Glu Ala Leu Glu Ile Val Gly Leu Ala Asp Tyr Ala Glu  
115 120 125

Arg Gln Ile Ser Gln Leu Ser Gly Gly Gln Phe Gln Arg Val Leu Ile  
130 135 140

30 Ala Arg Cys Leu Val Gln Glu Ala Asp Tyr Ile Leu Leu Asp Glu Pro  
145 150 155 160

35 Phe Ala Gly Ile Asp Ser Val Ser Glu Glu Ile Ile Met Asn Thr Leu  
165 170 175

Arg Asp Leu Lys Lys Ala Gly Lys Thr Val Leu Ile Val His His Asp  
180 185 190

40 Leu Ser Lys Ile Pro His Tyr Phe Asp Gln Val Leu Leu Val Asn Arg  
195 200 205

Glu Val Ile Ala Phe Gly Pro Thr Lys Glu Thr Phe Thr Glu Thr Asn  
210 215 220

45 Leu Lys Glu Ala Tyr Gly Asn Gln Leu Phe Phe Asn Gly Gly Asp Leu  
225 230 235 240

50

<210> 171

<211> 740

55 <212> PRT

<213> Streptococcus pneumoniae



<400> 171  
Met Pro Lys Glu Val Asn Leu Thr Gly Glu Glu Val Val Ala Leu Thr  
1 5 10 15

5 Lys Glu Tyr Leu Thr Glu Glu Asp Val His Phe Val His Lys Ala Leu  
20 25 30

Val Tyr Ala Val Glu Cys His Ser Gly Gln Tyr Arg Lys Ser Gly Glu  
35 40 45

10 Pro Tyr Ile Ile His Pro Ile Gln Val Ala Gly Ile Leu Ala Lys Leu  
50 55 60

15 Lys Leu Asp Ala Val Thr Val Ala Cys Gly Phe Leu His Asp Val Val  
65 70 75 80

Glu Asp Thr Asp Ala Thr Leu Asp Asp Leu Glu Arg Glu Phe Gly Pro  
85 90 95

20 Asp Val Arg Val Ile Val Asp Gly Val Thr Lys Leu Gly Lys Val Glu  
100 105 110

Tyr Lys Ser Ile Glu Glu Gln Leu Ala Glu Asn His Arg Lys Met Leu  
115 120 125

25 Met Ala Met Ser Glu Asp Ile Arg Val Ile Leu Val Lys Leu Ser Asp  
130 135 140

30 Arg Leu His Asn Met Arg Thr Leu Lys His Leu Arg Lys Asp Lys Gln  
145 150 155 160

Glu Arg Ile Ser Lys Glu Thr Met Glu Ile Tyr Ala Pro Leu Ala His  
165 170 175

35 Arg Leu Gly Ile Ser Ser Val Lys Trp Glu Leu Glu Asp Leu Ser Phe  
180 185 190

Arg Tyr Leu Asn Pro Thr Glu Phe Tyr Lys Ile Thr His Met Met Lys  
195 200 205

40 Glu Lys Arg Arg Glu Arg Glu Ala Leu Val Asp Glu Val Val Thr Lys  
210 215 220

45 Leu Glu Glu Tyr Thr Thr Glu Arg His Leu Lys Gly Lys Ile Tyr Gly  
225 230 235 240

Arg Pro Lys His Ile Tyr Ser Ile Phe Arg Lys Met Gln Asp Lys Arg  
245 250 255

50 Lys Arg Phe Glu Glu Ile Tyr Asp Leu Ile Ala Ile Arg Cys Ile Leu  
260 265 270

Asp Thr Gln Ser Asp Val Tyr Ala Met Leu Gly Tyr Val His Glu Phe  
275 280 285

55 Trp Lys Pro Met Pro Gly Arg Phe Lys Asp Tyr Ile Ala Asn Arg Lys  
290 295 300

Ala Asn Gly Tyr Gln Ser Ile His Thr Thr Val Tyr Gly Pro Lys Gly  
 305 310 315 320  
 5 Pro Ile Glu Phe Gln Ile Arg Thr Lys Glu Met His Glu Val Ala Glu  
 325 330 335  
 Tyr Gly Val Ala Ala His Trp Ala Tyr Lys Lys Gly Ile Lys Gly Gln  
 340 345 350  
 10 Val Asn Ser Lys Glu Ser Ala Ile Gly Met Asn Trp Ile Lys Glu Met  
 355 360 365  
 15 Met Glu Leu Gln Asp Gln Ala Asp Asp Ala Lys Glu Phe Val Asp Ser  
 370 375 380  
 Val Lys Glu Asn Tyr Leu Ala Glu Glu Ile Tyr Val Phe Thr Pro Asp  
 385 390 395 400  
 20 Gly Ala Val Arg Ser Leu Pro Lys Asp Ser Gly Pro Ile Asp Phe Ala  
 405 410 415  
 Tyr Glu Ile His Thr Lys Val Gly Glu Lys Ala Thr Gly Ala Lys Val  
 420 425 430  
 25 Asn Gly Arg Met Val Pro Leu Thr Thr Lys Leu Lys Thr Gly Asp Gln  
 435 440 445  
 30 Val Glu Ile Ile Ala Asn Pro Asn Ser Phe Gly Pro Ser Arg Asp Trp  
 450 455 460  
 Leu Asn Met Val Lys Thr Ser Lys Ala Arg Asn Lys Ile Arg Gln Phe  
 465 470 475 480  
 35 Phe Lys Asn Gln Asp Lys Glu Leu Ser Val Asn Lys Gly Arg Glu Met  
 485 490 495  
 Leu Met Ala Gln Phe Gln Glu Asn Gly Tyr Val Ala Asn Lys Phe Met  
 500 505 510  
 40 Asp Lys Arg His Met Asp Gln Val Leu Gln Lys Thr Ser Tyr Lys Thr  
 515 520 525  
 Glu Asp Ser Leu Phe Ala Ala Ile Gly Phe Gly Glu Ile Gly Ala Ile  
 530 535 540  
 45 Thr Val Phe Asn Arg Leu Thr Glu Lys Glu Arg Arg Glu Glu Glu Arg  
 545 550 555 560  
 50 Ala Lys Ala Lys Ala Glu Ala Glu Glu Leu Val Lys Gly Gly Glu Val  
 565 570 575  
 Lys Val Glu Asn Lys Glu Thr Leu Lys Val Lys His Glu Gly Gly Val  
 580 585 590  
 55 Val Ile Glu Gly Ala Ser Gly Leu Leu Val Arg Ile Ala Lys Cys Cys  
 595 600 605

Asn Pro Val Pro Gly Asp Asp Ile Val Gly Tyr Ile Thr Lys Gly Arg  
 610 615 620

5 Gly Val Ala Ile His Arg Val Asp Cys Met Asn Leu Arg Ala Gln Glu  
 625 630 635 640

Asn Tyr Glu Gln Arg Leu Leu Asp Val Glu Trp Glu Asp Gln Tyr Ser  
 645 650 655

10 Ser Ser Asn Lys Glu Tyr Leu Ala His Ile Asp Ile Tyr Gly Leu Asn  
 660 665 670

Arg Thr Gly Leu Leu Asn Asp Val Leu Gln Val Leu Ser Asn Thr Thr  
 675 680 685

Lys Asn Ile Ser Thr Val Asn Ala Gln Pro Thr Lys Asp Met Lys Phe  
 690 695 700

20 Ala Asn Ile His Val Ser Phe Gly Ile Ala Asn Leu Ser Thr Leu Thr  
 705 710 715 720

Thr Val Val Asp Lys Ile Lys Ser Val Pro Glu Val Tyr Ser Val Lys  
 725 730 735

25 Arg Thr Asn Gly  
 740

30 <210> 172  
 <211> 492  
 <212> PRT  
 <213> Streptococcus pneumoniae

35 <400> 172  
 Met Ser Asn Trp Asp Thr Lys Phe Leu Lys Lys Gly Phe Thr Phe Asp  
 1 5 10 15

40 Asp Val Leu Leu Ile Pro Ala Glu Ser His Val Leu Pro Asn Asp Ala  
 20 25 30

Asp Leu Thr Thr Lys Leu Ala Asp Asn Leu Thr Leu Asn Ile Pro Ile  
 35 40 45

45 Ile Thr Ala Ala Met Asp Thr Val Thr Glu Ser Gln Met Ala Ile Ala  
 50 55 60

Ile Ala Arg Ala Gly Gly Leu Gly Val Ile His Lys Asn Met Ser Ile  
 65 70 75 80

50 Ala Gln Gln Ala Asp Glu Val Arg Lys Val Lys Arg Ser Glu Asn Gly  
 85 90 95

Val Ile Ile Asp Pro Phe Phe Leu Thr Pro Glu His Thr Ile Ala Glu  
 100 105 110

55 Ala Asp Glu Leu Met Gly Arg Tyr Arg Ile Ser Gly Val Pro Val Val

|    | 115   | 120 | 125 |
|----|---|-----|-----|
|    | Glu Thr Leu Glu Asn Arg Lys Leu Val Gly Ile Leu Thr Asn Arg Asp |     |     |
|    | 130   | 135 | 140 |
| 5  | Leu Arg Phe Ile Ser Asp Tyr Asn Gln Pro Ile Ser Asn His Met Thr |     |     |
|    | 145   | 150 | 155 |
|    | Ser Glu Asn Leu Val Thr Ala Pro Val Gly Thr Asp Leu Ala Thr Ala |     |     |
| 10 |   | 165 | 170 |
|    | Glu Ser Ile Leu Gln Glu His Arg Ile Glu Lys Leu Pro Leu Val Asp |     |     |
|    | 180   | 185 | 190 |
| 15 | Glu Glu Gly Ser Leu Ser Gly Leu Ile Thr Ile Lys Asp Ile Glu Lys |     |     |
|    | 195   | 200 | 205 |
|    | Val Ile Glu Phe Pro Asn Ala Ala Lys Asp Glu Phe Gly Arg Leu Leu |     |     |
| 20 |   | 215 | 220 |
|    | Val Ala Gly Ala Val Gly Val Thr Ser Asp Thr Phe Glu Arg Ala Glu |     |     |
|    | 225   | 230 | 235 |
| 25 | Ala Leu Phe Glu Ala Gly Ala Asp Ala Ile Val Ile Asp Thr Ala His |     |     |
|    | 245   | 250 | 255 |
|    | Gly His Ser Ala Gly Val Leu Arg Lys Ile Ala Glu Ile Arg Ala His |     |     |
|    | 260   | 265 | 270 |
| 30 | Phe Pro Asp Arg Thr Leu Ile Ala Gly Asn Ile Ala Thr Ala Glu Gly |     |     |
|    | 275   | 280 | 285 |
|    | Ala Arg Ala Leu Tyr Glu Ala Gly Val Asp Val Val Lys Val Gly Ile |     |     |
| 35 |   | 295 | 300 |
|    | Gly Pro Gly Ser Ile Cys Thr Thr Arg Val Ile Ala Gly Val Gly Val |     |     |
|    | 305   | 310 | 315 |
| 40 | Pro Gln Val Thr Ala Ile Tyr Asp Ala Ala Ala Val Ala Arg Glu Tyr |     |     |
|    | 325   | 330 | 335 |
|    | Gly Lys Thr Ile Ile Ala Asp Gly Gly Ile Lys Tyr Ser Gly Asp Ile |     |     |
|    | 340   | 345 | 350 |
| 45 | Val Lys Ala Leu Ala Ala Gly Gly Asn Ala Val Met Leu Gly Ser Met |     |     |
|    | 355   | 360 | 365 |
|    | Phe Ala Gly Thr Asp Glu Ala Pro Gly Glu Thr Glu Ile Phe Gln Gly |     |     |
| 50 |   | 375 | 380 |
|    | Arg Lys Phe Lys Thr Tyr Arg Gly Met Gly Ser Ile Ala Ala Met Lys |     |     |
|    | 385   | 390 | 395 |
| 55 | Lys Gly Ser Ser Asp Arg Tyr Phe Gln Gly Ser Val Asn Glu Ala Asn |     |     |
|    | 405   | 410 | 415 |
|    | Lys Leu Val Pro Glu Gly Ile Glu Gly Arg Val Ala Tyr Lys Gly Ala |     |     |

420                      425                      430  
 Ala Ala Asp Ile Val Phe Gln Met Ile Gly Gly Ile Arg Ser Gly Met  
                     435                      440                      445  
 5 Gly Tyr Cys Gly Ala Ala Asn Leu Lys Glu Leu His Asp Asn Ala Gln  
                     450                      455                      460  
 Phe Ile Glu Met Ser Gly Ala Gly Leu Lys Glu Ser His Pro His Asp  
 10 465                      470                      475                      480  
 Val Gln Ile Thr Asn Glu Ala Pro Asn Tyr Ser Met  
                     485                      490  
 15  
 <210> 173  
 <211> 648  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 20  
 <400> 173  
 Met Thr Glu Glu Ile Lys Asn Leu Gln Ala Gln Asp Tyr Asp Ala Ser  
                     1                      5                      10                      15  
 25 Gln Ile Gln Val Leu Glu Gly Leu Glu Ala Val Arg Met Arg Pro Gly  
                     20                      25                      30  
 Met Tyr Ile Gly Ser Thr Ser Lys Glu Gly Leu His His Leu Val Trp  
                     35                      40                      45  
 30 Glu Ile Val Asp Asn Ser Ile Asp Glu Ala Leu Ala Gly Phe Ala Ser  
                     50                      55                      60  
 His Ile Gln Val Phe Ile Glu Pro Asp Asp Ser Ile Thr Val Val Asp  
 35 65                      70                      75                      80  
 Asp Gly Arg Gly Ile Pro Val Asp Ile Gln Glu Lys Thr Gly Arg Pro  
                     85                      90                      95  
 40 Ala Val Glu Thr Val Phe Thr Val Leu His Ala Gly Gly Lys Phe Gly  
                     100                      105                      110  
 Gly Gly Gly Tyr Lys Val Ser Gly Gly Leu His Gly Val Gly Ser Ser  
                     115                      120                      125  
 45 Val Val Asn Ala Leu Ser Thr Gln Leu Asp Val His Val His Lys Asn  
                     130                      135                      140  
 Gly Lys Ile His Tyr Gln Glu Tyr Arg Arg Gly His Val Val Ala Asp  
 50 145                      150                      155                      160  
 Leu Glu Ile Val Gly Asp Thr Asp Lys Thr Gly Thr Thr Val His Phe  
                     165                      170                      175  
 55 Thr Pro Asp Pro Lys Ile Phe Thr Glu Thr Thr Ile Phe Asp Phe Asp  
                     180                      185                      190

Lys Leu Asn Lys Arg Ile Gln Glu Leu Ala Phe Leu Asn Arg Gly Leu  
 195 200 205  
 5 Gln Ile Ser Ile Thr Asp Lys Arg Gln Gly Leu Glu Gln Thr Lys His  
 210 215 220  
 Tyr His Tyr Glu Gly Gly Ile Ala Ser Tyr Val Glu Tyr Ile Asn Glu  
 225 230 235 240  
 10 Asn Lys Asp Val Ile Phe Asp Thr Pro Ile Tyr Thr Asp Gly Glu Met  
 245 250 255  
 Asp Asp Ile Thr Val Glu Val Ala Met Gln Tyr Thr Thr Gly Tyr His  
 260 265 270  
 15 Glu Asn Val Met Ser Phe Ala Asn Asn Ile His Thr His Glu Gly Gly  
 275 280 285  
 Thr His Glu Gln Gly Phe Arg Thr Ala Leu Thr Arg Val Ile Asn Asp  
 290 295 300  
 Tyr Ala Arg Lys Asn Lys Leu Leu Lys Asp Asn Glu Asp Asn Leu Thr  
 305 310 315 320  
 25 Gly Glu Asp Val Arg Glu Gly Leu Thr Ala Val Ile Ser Val Lys His  
 325 330 335  
 Pro Asn Pro Gln Phe Glu Gly Gln Thr Lys Thr Lys Leu Gly Asn Ser  
 340 345 350  
 30 Glu Val Val Lys Ile Thr Asn Arg Leu Phe Ser Glu Ala Phe Ser Asp  
 355 360 365  
 Phe Leu Met Glu Asn Pro Gln Ile Ala Lys Arg Ile Val Glu Lys Gly  
 370 375 380  
 35 Ile Leu Ala Ala Lys Ala Arg Val Ala Ala Lys Arg Ala Arg Glu Val  
 385 390 395 400  
 40 Thr Arg Lys Lys Ser Gly Leu Glu Ile Ser Asn Leu Pro Gly Lys Leu  
 405 410 415  
 Ala Asp Cys Ser Ser Asn Asn Pro Ala Glu Thr Glu Leu Phe Ile Val  
 420 425 430  
 45 Glu Gly Asp Ser Ala Gly Gly Ser Ala Lys Ser Gly Arg Asn Arg Glu  
 435 440 445  
 Phe Gln Ala Ile Leu Pro Ile Arg Gly Lys Ile Leu Asn Val Glu Lys  
 450 455 460  
 50 Ala Ser Met Asp Lys Ile Leu Ala Asn Glu Glu Ile Arg Ser Leu Phe  
 465 470 475 480  
 55 Thr Ala Met Gly Thr Gly Phe Gly Ala Glu Phe Asp Val Ser Lys Ala  
 485 490 495

Arg Tyr Gln Lys Leu Val Leu Met Thr Asp Ala Asp Val Asp Gly Ala  
 500 505 510  
 5 His Ile Arg Thr Leu Leu Leu Thr Leu Ile Tyr Arg Tyr Met Lys Pro  
 515 520 525  
 Ile Leu Glu Ala Gly Tyr Val Tyr Ile Ala Gln Pro Pro Ile Tyr Gly  
 530 535 540  
 10 Val Lys Val Gly Ser Glu Ile Lys Glu Tyr Ile Gln Pro Gly Ala Asp  
 545 550 555 560  
 Gln Glu Ile Lys Leu Gln Glu Ala Leu Ala Arg Tyr Ser Glu Gly Arg  
 565 570 575  
 15 Thr Lys Pro Thr Ile Gln Arg Tyr Lys Gly Leu Gly Glu Met Asp Asp  
 580 585 590  
 20 His Gln Leu Trp Glu Thr Thr Met Asp Pro Glu His Arg Leu Met Ala  
 595 600 605  
 Arg Val Ser Val Asp Asp Ala Ala Glu Ala Asp Lys Ile Phe Asp Met  
 610 615 620  
 25 Leu Met Gly Asp Arg Val Glu Pro Arg Arg Glu Phe Ile Glu Glu Asn  
 625 630 635 640  
 Ala Val Tyr Ser Thr Leu Asp Val  
 645  
 30  
 <210> 174  
 <211> 88  
 <212> PRT  
 35 <213> Streptococcus pneumoniae  
 <400> 174  
 Met Gly Phe Thr Glu Glu Thr Val Arg Phe Lys Leu Asp Asp Ser Asn  
 1 5 10 15  
 40 Lys Lys Glu Ile Ser Glu Thr Leu Thr Asp Val Tyr Ala Ser Leu Asn  
 20 25 30  
 45 Asp Lys Gly Tyr Asn Pro Ile Asn Gln Ile Val Gly Tyr Val Leu Ser  
 35 40 45  
 Gly Asp Pro Ala Tyr Val Pro Arg Tyr Asn Asn Ala Arg Asn Gln Ile  
 50 55 60  
 50 Arg Lys Tyr Glu Arg Asp Glu Ile Val Glu Glu Leu Val Arg Tyr Tyr  
 65 70 75 80  
 Leu Lys Gly Gln Gly Val Asp Leu  
 85  
 55  
 <210> 175

<211> 198  
 <212> PRT  
 <213> Streptococcus pneumoniae

5 <400> 175  
 Met Val Asn Tyr Pro His Lys Val Ser Ser Gln Asp Arg Gln Thr Ser  
 1 5 10 15

10 Leu Ser Gln Pro Lys Asn Phe Ala Asn Arg Gly Met Ser Phe Glu Lys  
 20 25 30

Met Ile Asn Ala Thr Asn Asp Tyr Tyr Leu Ser Gln Gly Leu Ala Val  
 35 40 45

15 Ile His Lys Lys Pro Thr Pro Ile Gln Ile Val Gln Val Asp Tyr Pro  
 50 55 60

Gln Arg Ser Arg Ala Lys Ile Val Glu Ala Tyr Phe Arg Gln Ala Ser  
 65 70 75 80

20 Thr Thr Asp Tyr Ser Gly Val Tyr Asn Gly Tyr Tyr Ile Asp Phe Glu  
 85 90 95

Val Lys Glu Thr Lys Gln Lys Arg Ala Ile Pro Met Lys Asn Phe His  
 100 105 110

25 Pro His Gln Ile Gln His Met Glu Gln Val Leu Ala Gln Gln Gly Ile  
 115 120 125

30 Cys Phe Val Leu Leu His Phe Ser Ser Gln Gln Glu Thr Tyr Leu Leu  
 130 135 140

Pro Ala Phe Asp Leu Ile Arg Phe Tyr His Gln Asp Lys Gly Gln Lys  
 145 150 155 160

35 Ser Met Pro Leu Glu Tyr Ile Arg Glu Tyr Gly Tyr Glu Ile Lys Ala  
 165 170 175

Gly Ala Phe Pro Gln Ile Pro Tyr Leu Asn Val Ile Lys Glu His Leu  
 180 185 190

40 Leu Gly Gly Lys Thr Arg  
 195

45 <210> 176  
 <211> 288  
 <212> PRT  
 <213> Streptococcus pneumoniae

50 <400> 176  
 Met Ala Leu Phe Ser Lys Lys Asp Lys Tyr Ile Arg Ile Asn Pro Asn  
 1 5 10 15

55 Arg Ser Val Arg Glu Lys Pro Gln Ala Lys Pro Glu Val Pro Asp Glu  
 20 25 30



Leu Phe Ser Gln Cys Pro Gly Cys Lys His Thr Ile Tyr Gln Lys Asp  
                   35                                  40                                  45

5    Leu Gly Ser Glu Arg Ile Cys Pro His Cys Ser Tyr Thr Phe Arg Ile  
                   50                                  55                                  60

      Ser Ala Gln Glu Arg Leu Ala Leu Thr Ile Asp Met Gly Thr Phe Lys  
           65                                  70                                  75                                  80

10    Glu Leu Phe Thr Gly Ile Glu Ser Lys Asp Pro Leu His Phe Pro Gly  
                                   85                                  90                                  95

      Tyr Gln Lys Lys Leu Ala Ser Met Arg Glu Lys Thr Gly Leu His Glu  
                                   100                                  105                                  110

15    Ala Val Val Thr Gly Thr Ala Leu Ile Lys Gly Gln Thr Val Ala Leu  
                   115                                  120                                  125

      Gly Ile Met Asp Ser Asn Phe Ile Met Ala Ser Met Gly Thr Val Val  
           130                                  135                                  140

20    Gly Glu Lys Ile Thr Arg Leu Phe Glu Tyr Ala Thr Val Glu Lys Leu  
           145                                  150                                  155                                  160

      Pro Val Val Leu Phe Thr Ala Ser Gly Gly Ala Arg Met Gln Glu Gly  
                                   165                                  170                                  175

      Ile Met Ser Leu Met Gln Met Ala Lys Ile Ser Ala Ala Val Lys Arg  
                                   180                                  185                                  190

30    His Ser Asn Ala Gly Leu Phe Tyr Leu Thr Ile Leu Thr Asp Pro Thr  
                   195                                  200                                  205

      Thr Gly Gly Val Thr Ala Ser Phe Ala Met Glu Gly Asp Ile Ile Leu  
           210                                  215                                  220

      Ala Glu Pro Gln Ser Leu Val Gly Phe Ala Gly Arg Arg Val Ile Glu  
           225                                  230                                  235                                  240

40    Asn Thr Val Arg Glu Ser Leu Pro Glu Asp Phe Gln Lys Ala Glu Phe  
                                   245                                  250                                  255

      Leu Leu Glu His Gly Phe Val Asp Ala Ile Val Lys Arg Arg Asp Leu  
                                   260                                  265                                  270

45    Pro Asp Thr Ile Ala Ser Leu Val Arg Leu His Gly Gly Ser Pro Arg  
                   275                                  280                                  285

50

55    <210> 177  
       <211> 139  
       <212> PRT  
       <213> Streptococcus pneumoniae

<400> 177  
 Met Arg Ile Met Gly Leu Asp Val Gly Ser Lys Thr Val Gly Val Ala  
   1                  5                  10                  15  
 5 Ile Ser Asp Pro Leu Gly Phe Thr Ala Gln Gly Leu Glu Ile Ile Gln  
                   20                  25                  30  
 Ile Asn Glu Glu Gln Gly Gln Phe Gly Ser Asp Arg Val Lys Glu Leu  
                   35                  40                  45  
 10 Val Asp Thr Tyr Lys Val Glu Arg Phe Val Val Gly Leu Pro Lys Asn  
                   50                  55                  60  
 15 Met Asn Asn Thr Ser Gly Pro Arg Val Glu Ala Ser Gln Ala Tyr Gly  
       65                  70                  75                  80  
 Ala Lys Leu Glu Glu Phe Phe Gly Leu Pro Val Asp Tyr Gln Asp Glu  
                   85                  90                  95  
 20 Arg Leu Thr Thr Val Ala Ala Glu Arg Met Leu Ile Glu Gln Ala Asp  
                   100                  105                  110  
 Ile Ser Arg Asn Lys Arg Lys Lys Val Ile Asp Lys Leu Ala Ala Gln  
                   115                  120                  125  
 25 Leu Ile Leu Gln Asn Tyr Leu Asp Arg Lys Phe  
                   130                  135  
 30 <210> 178  
     <211> 398  
     <212> PRT  
     <213> Streptococcus pneumoniae  
 35 <400> 178  
 Met Ala Lys Leu Thr Val Lys Asp Val Asp Leu Lys Gly Lys Lys Val  
   1                  5                  10                  15  
 40 Leu Val Arg Val Asp Phe Asn Val Pro Leu Lys Asp Gly Val Ile Thr  
                   20                  25                  30  
 Asn Asp Asn Arg Ile Thr Ala Ala Leu Pro Thr Ile Lys Tyr Ile Ile  
                   35                  40                  45  
 45 Glu Gln Gly Gly Arg Ala Ile Leu Phe Ser His Leu Gly Arg Val Lys  
                   50                  55                  60  
 Glu Glu Ala Asp Lys Ala Gly Lys Ser Leu Ala Pro Val Ala Ala Asp  
   65                  70                  75                  80  
 50 Leu Ala Ala Lys Leu Gly Gln Asp Val Val Phe Pro Gly Val Thr Arg  
                   85                  90                  95  
 Gly Ala Glu Leu Glu Ala Ala Ile Asn Ala Leu Glu Asp Gly Gln Val  
                   100                  105                  110  
 55 Leu Leu Val Glu Asn Thr Arg Tyr Glu Asp Val Asp Gly Lys Lys Glu

|    | 115   | 120 | 125 |
|----|---|-----|-----|
|    | Ser Lys Asn Asp Pro Glu Leu Gly Lys Tyr Trp Ala Ser Leu Gly Asp |     |     |
|    | 130   | 135 | 140 |
| 5  | Gly Ile Phe Val Asn Asp Ala Phe Gly Thr Ala His Arg Ala His Ala |     |     |
|    | 145   | 150 | 155 |
|    | Ser Asn Val Gly Ile Ser Ala Asn Val Glu Lys Ala Val Ala Gly Phe |     |     |
| 10 |   | 165 | 170 |
|    | Leu Leu Glu Asn Glu Ile Ala Tyr Ile Gln Glu Ala Val Glu Thr Pro |     |     |
|    |   | 180 | 185 |
| 15 | Glu Arg Pro Phe Val Ala Ile Leu Gly Gly Ser Lys Val Ser Asp Lys |     |     |
|    |   | 195 | 200 |
|    | Ile Gly Val Ile Glu Asn Leu Leu Glu Lys Ala Asp Lys Val Leu Ile |     |     |
|    | 210   | 215 | 220 |
| 20 | Gly Gly Gly Met Thr Tyr Thr Phe Tyr Lys Ala Gln Gly Ile Glu Ile |     |     |
|    | 225   | 230 | 235 |
|    | Gly Asn Ser Leu Val Glu Glu Asp Lys Leu Asp Val Ala Lys Ala Leu |     |     |
| 25 |   | 245 | 250 |
|    | Leu Glu Lys Ala Asn Gly Lys Leu Ile Leu Pro Val Asp Ser Lys Glu |     |     |
|    |   | 260 | 265 |
| 30 | Ala Asn Ala Phe Ala Gly Tyr Thr Glu Val Arg Asp Thr Glu Gly Glu |     |     |
|    |   | 275 | 280 |
|    | Ala Val Ser Glu Gly Phe Leu Gly Leu Asp Ile Gly Pro Lys Ser Ile |     |     |
|    | 290   | 295 | 300 |
| 35 | Ala Lys Phe Asp Glu Ala Leu Thr Gly Ala Lys Thr Val Val Trp Asn |     |     |
|    | 305   | 310 | 315 |
|    | Gly Pro Met Gly Val Phe Glu Asn Pro Asp Phe Gln Ala Gly Thr Ile |     |     |
| 40 |   | 325 | 330 |
|    | Gly Val Met Asp Ala Ile Val Lys Gln Pro Gly Val Lys Ser Ile Ile |     |     |
|    |   | 340 | 345 |
| 45 | Gly Gly Gly Asp Ser Ala Ala Ala Ala Ile Asn Leu Gly Arg Ala Asp |     |     |
|    |   | 355 | 360 |
|    | Lys Phe Ser Trp Ile Ser Thr Gly Gly Gly Ala Ser Met Glu Leu Leu |     |     |
|    | 370   | 375 | 380 |
| 50 | Glu Gly Lys Val Leu Pro Gln Leu Ala Ala Leu Thr Glu Lys         |     |     |
|    | 385   | 390 | 395 |
| 55 | <210> 179   |     |     |
|    | <211> 165   |     |     |
|    | <212> PRT   |     |     |

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 179

5 Met Leu Lys Ser Glu Lys Gln Ser Arg Tyr Gln Met Leu Asn Glu Glu  
 1 5 10 15  
 Leu Ser Phe Leu Leu Glu Gly Glu Thr Asn Val Leu Ala Asn Leu Ser  
 20 25 30  
 10 Asn Ala Ser Ala Leu Ile Lys Ser Arg Phe Pro Asn Thr Val Phe Ala  
 35 40 45  
 Gly Phe Tyr Leu Phe Asp Gly Lys Glu Leu Val Leu Gly Pro Phe Gln  
 50 55 60  
 15 Gly Gly Val Ser Cys Ile Arg Ile Ala Leu Gly Lys Gly Val Cys Gly  
 65 70 75 80  
 Glu Ala Ala His Phe Gln Glu Thr Val Ile Val Gly Asp Val Thr Thr  
 85 90 95  
 20 Tyr Leu Asn Tyr Ile Ser Cys Asp Ser Leu Ala Lys Ser Glu Ile Val  
 100 105 110  
 25 Val Pro Met Met Lys Asn Gly Gln Leu Leu Gly Val Leu Asp Leu Asp  
 115 120 125  
 Ser Ser Glu Ile Glu Asp Tyr Asp Ala Met Asp Arg Asp Tyr Leu Glu  
 130 135 140  
 30 Gln Phe Val Ala Ile Leu Leu Glu Lys Thr Ala Trp Asp Phe Thr Met  
 145 150 155 160  
 Phe Glu Glu Lys Ser  
 165  
 35

&lt;210&gt; 180

&lt;211&gt; 209

40 &lt;212&gt; PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 180

45 Met Thr Ile Glu Leu Leu Thr Pro Phe Thr Lys Val Glu Leu Glu Pro  
 1 5 10 15  
 Glu Ile Lys Glu Lys Lys Arg Lys Gln Val Gly Ile Leu Gly Gly Asn  
 20 25 30  
 50 Phe Asn Pro Val His Asn Ala His Leu Ile Val Ala Asp Gln Val Arg  
 35 40 45  
 Gln Gln Leu Gly Leu Asp Gln Val Leu Leu Met Pro Glu Tyr Gln Pro  
 50 55 60  
 55 Pro His Val Asp Lys Lys Glu Thr Ile Pro Glu His His Arg Leu Lys  
 65 70 75 80

Met Leu Glu Leu Ala Ile Glu Gly Ile Asp Gly Leu Val Ile Glu Thr  
85 90 95

5 Ile Glu Leu Glu Arg Lys Gly Ile Ser Tyr Thr Tyr Asp Thr Met Lys  
100 105 110

Ile Leu Thr Glu Lys Asn Pro Asp Thr Asp Tyr Tyr Phe Ile Ile Gly  
115 120 125

10 Ala Asp Met Val Asp Tyr Leu Pro Lys Trp Tyr Arg Ile Asp Glu Leu  
130 135 140

Val Asp Met Val Gln Phe Val Gly Val Gln Arg Pro Arg Tyr Lys Val  
15 145 150 155 160

Gly Thr Ser Tyr Pro Val Ile Trp Val Asp Val Pro Leu Met Asp Ile  
165 170 175

20 Ser Ser Ser Met Val Arg Ala Phe Leu Ala Gln Gly Arg Lys Pro Asn  
180 185 190

Phe Leu Leu Pro Gln Pro Val Leu Asp Tyr Ile Glu Lys Glu Gly Leu  
195 200 205

25 Tyr

30 <210> 181  
<211> 255  
<212> PRT  
<213> Streptococcus pneumoniae

35 <400> 181  
Met Asn Ile Ala Lys Ile Val Arg Glu Ala Arg Glu Gln Ser Arg Leu  
1 5 10 15

Thr Thr Leu Asp Phe Ala Thr Gly Ile Phe Asp Glu Phe Ile Gln Leu  
40 20 25 30

His Gly Asp Arg Ser Phe Arg Asp Asp Gly Ala Val Val Gly Gly Ile  
35 40 45

45 Gly Trp Leu Gly Asp Gln Ala Val Thr Val Val Gly Ile Gln Lys Gly  
50 55 60

Lys Ser Leu Gln Asp Asn Leu Lys Arg Asn Phe Gly Gln Pro His Pro  
65 70 75 80

50 Glu Gly Tyr Arg Lys Ala Leu Arg Leu Met Lys Gln Ala Glu Lys Phe  
85 90 95

Gly Arg Pro Val Val Thr Phe Ile Asn Thr Ala Gly Ala Tyr Pro Gly  
55 100 105 110

Val Gly Ala Glu Glu Arg Gly Gln Gly Glu Ala Ile Ala Arg Asn Leu

115                                      120                                      125  
 Met Glu Met Ser Asp Leu Lys Val Pro Ile Ile Ala Ile Ile Ile Gly  
       130                                      135                                      140  
 5                                      Glu Gly Gly Ser Gly Gly Ala Leu Ala Leu Ala Val Ala Asp Arg Val  
       145                                      150                                      155                                      160  
 10                                      Trp Met Leu Glu Asn Ser Ile Tyr Ala Ile Leu Ser Pro Glu Gly Phe  
                                     165                                      170                                      175  
                                     Ala Ser Ile Leu Trp Lys Asp Gly Thr Arg Ala Met Glu Ala Ala Glu  
                                     180                                      185                                      190  
 15                                      Leu Met Lys Ile Thr Ser His Glu Leu Leu Glu Met Asp Val Val Asp  
                                     195                                      200                                      205  
                                     Lys Val Ile Ser Glu Val Gly Leu Ser Ser Lys Glu Leu Ile Lys Ser  
                                     210                                      215                                      220  
 20                                      Val Lys Lys Glu Leu Gln Thr Glu Leu Ala Arg Leu Ser Gln Lys Pro  
                                     225                                      230                                      235                                      240  
 25                                      Leu Glu Glu Leu Leu Glu Glu Arg Tyr Gln Arg Phe Arg Lys Tyr  
                                     245                                      250                                      255  
                                     <210> 182  
                                     <211> 169  
 30                                      <212> PRT  
                                     <213> Streptococcus pneumoniae  
                                     <400> 182  
 35                                      Met Ile Ile Lys Val Glu Met Ala Asp Val Glu Val Leu Ala Lys Ile  
                                     1                                      5                                      10                                      15  
                                     Ala Lys Gln Thr Phe Arg Glu Thr Phe Ala Tyr Asp Asn Thr Glu Glu  
                                     20                                      25                                      30  
 40                                      Gln Leu Gln Glu Tyr Phe Glu Glu Ala Tyr Ser Leu Lys Thr Leu Ser  
                                     35                                      40                                      45  
                                     Thr Glu Leu Gly Asn Pro Asp Ser Glu Thr Tyr Phe Ile Met His Glu  
                                     50                                      55                                      60  
 45                                      Glu Glu Ile Ala Gly Phe Leu Lys Val Asn Trp Gly Ser Ala Gln Thr  
                                     65                                      70                                      75                                      80  
 50                                      Glu Arg Glu Leu Glu Asp Ala Phe Glu Ile Gln Arg Leu Tyr Val Leu  
                                     85                                      90                                      95  
                                     Gln Lys Phe Gln Gly Phe Gly Leu Gly Lys Gln Leu Phe Glu Phe Ala  
                                     100                                      105                                      110  
 55                                      Leu Glu Leu Ala Thr Lys Asn Ser Phe Ser Trp Ala Trp Leu Gly Val  
                                     115                                      120                                      125

Trp Glu His Asn Thr Lys Ala Gln Ala Phe Tyr Asn Arg Tyr Gly Phe  
 130 135 140

5 Glu Lys Phe Ser Gln His His Phe Met Val Gly Gln Lys Val Asp Thr  
 145 150 155 160

Asp Trp Leu Leu Arg Lys Lys Leu Arg  
 165

10 <210> 183  
 <211> 529  
 <212> PRT  
 <213> Streptococcus pneumoniae

15 <400> 183  
 Met Leu Arg Gly Thr Ala Leu Leu Thr Ala Ser Asn Phe Ile Ser Arg  
 1 5 10 15

20 Leu Leu Gly Ala Val Tyr Ile Ile Pro Trp Tyr Ile Trp Met Gly Ala  
 20 25 30

Tyr Ala Ala Lys Ala Asn Gly Leu Phe Thr Met Gly Tyr Thr Ile Tyr  
 35 40 45

25 Ala Trp Phe Leu Leu Val Ser Thr Ala Gly Ile Pro Val Ala Val Ala  
 50 55 60

30 Lys Gln Val Ala Lys Tyr Asn Thr Met Arg Glu Glu Glu His Ser Phe  
 65 70 75 80

Ala Leu Ile Arg Ser Phe Leu Gly Phe Met Thr Gly Leu Gly Leu Val  
 85 90 95

35 Phe Ala Leu Val Leu Tyr Val Phe Ala Pro Trp Leu Ala Asp Leu Ser  
 100 105 110

Gly Val Gly Lys Asp Leu Ile Pro Ile Met Gln Ser Leu Ala Trp Gly  
 115 120 125

40 Val Leu Ile Phe Pro Ser Met Ser Val Ile Arg Gly Phe Phe Gln Gly  
 130 135 140

45 Met Asn Asn Leu Lys Pro Tyr Ala Met Ser Gln Ile Ala Glu Gln Val  
 145 150 155 160

Ile Arg Val Ile Trp Met Leu Leu Ala Thr Phe Ile Ile Met Lys Leu  
 165 170 175

50 Gly Ser Gly Asp Tyr Leu Ala Ala Val Thr Gln Ser Thr Phe Ala Ala  
 180 185 190

Phe Val Gly Met Val Ala Ser Phe Ala Val Leu Ile Tyr Phe Leu Ala  
 195 200 205

55 Gln Glu Ser Ser Leu Lys Arg Val Phe Glu Thr Gly Asp Lys Ile Asn  
 210 215 220

Ser Lys Arg Leu Leu Val Asp Thr Ile Lys Glu Ala Ile Pro Phe Ile  
 225 230 235 240  
 5 Leu Thr Gly Ser Ala Ile Gln Ile Phe Gln Ile Leu Asp Gln Leu Thr  
 245 250 255  
 Phe Ile Asn Ser Met Ser Trp Phe Thr Asn Tyr Ser Asn Glu Asp Leu  
 260 265 270  
 10 Val Val Met Phe Ser Tyr Phe Ser Ala Asn Pro Asn Lys Ile Thr Met  
 275 280 285  
 15 Ile Leu Ile Ser Val Gly Val Ser Ile Gly Ser Val Gly Leu Pro Leu  
 290 295 300  
 Leu Thr Glu Asn Tyr Val Lys Gly Asp Leu Lys Ala Ala Ser Arg Leu  
 305 310 315 320  
 20 Val Gln Asp Ser Leu Thr Leu Leu Phe Met Phe Leu Leu Pro Ala Thr  
 325 330 335  
 Val Gly Val Val Met Val Gly Glu Pro Leu Tyr Thr Val Phe Tyr Gly  
 340 345 350  
 25 Lys Pro Asp Ser Leu Ala Leu Gly Leu Phe Val Phe Ala Val Leu Gln  
 355 360 365  
 30 Ser Ile Ile Leu Gly Leu Tyr Met Val Leu Ser Pro Met Leu Gln Ala  
 370 375 380  
 Met Phe Arg Asn Arg Lys Ala Val Leu Tyr Phe Ile Tyr Gly Ser Ile  
 385 390 395 400  
 35 Ala Lys Leu Val Leu Gln Leu Pro Thr Ile Ala Leu Phe His Ser Tyr  
 405 410 415  
 Gly Pro Leu Ile Ser Thr Thr Ile Ala Leu Ile Ile Pro Asn Val Leu  
 420 425 430  
 40 Met Tyr Arg Asp Ile Cys Lys Val Thr Gly Val Lys Arg Lys Val Ile  
 435 440 445  
 45 Leu Lys Arg Thr Ile Leu Ile Ser Leu Leu Thr Leu Val Met Phe Leu  
 450 455 460  
 Leu Ile Gly Thr Ile Gln Trp Leu Leu Gly Phe Phe Phe Gln Pro Ser  
 465 470 475 480  
 50 Gly Arg Leu Trp Ser Phe Phe Tyr Val Ala Leu Val Gly Ala Met Gly  
 485 490 495  
 Gly Gly Leu Tyr Met Val Met Ser Leu Arg Thr Tyr Leu Leu Asp Lys  
 500 505 510  
 55 Val Ile Gly Lys Ala Gln Ala Asp Arg Leu Arg Ala Lys Phe Lys Leu  
 515 520 525



Ser

5  
 <210> 184  
 <211> 155  
 <212> PRT  
 <213> Streptococcus pneumoniae

10  
 <400> 184  
 Met Ser Asp Lys Ile Gly Leu Phe Thr Gly Ser Phe Asp Pro Met Thr  
 1 5 10 15

15 Asn Gly His Leu Asp Ile Ile Glu Arg Ala Ser Arg Leu Phe Asp Lys  
 20 25 30

Leu Tyr Val Gly Ile Phe Phe Asn Pro His Lys Gln Gly Phe Leu Pro  
 35 40 45

20 Ile Glu Asn Arg Lys Arg Gly Leu Glu Lys Ala Leu Gly His Leu Glu  
 50 55 60

25 Asn Val Glu Val Val Ala Ser His Asp Glu Leu Val Val Asp Val Ala  
 65 70 75 80

Lys Arg Leu Gly Ala Thr Cys Leu Val Arg Gly Leu Arg Asn Ala Ser  
 85 90 95

30 Asp Leu Gln Tyr Glu Ala Ser Phe Asp Tyr Tyr Asn His Gln Leu Ser  
 100 105 110

Ser Asp Ile Glu Thr Ile Tyr Leu His Ser Arg Pro Glu His Leu Tyr  
 115 120 125

35 Ile Ser Ser Ser Gly Val Arg Glu Leu Leu Lys Phe Gly Gln Asp Ile  
 130 135 140

40 Ala Cys Tyr Val Pro Glu Ser Ile Trp Arg Lys  
 145 150 155

45  
 <210> 185  
 <211> 143  
 <212> PRT  
 <213> Streptococcus pneumoniae

50  
 <400> 185  
 Met Thr Ile Leu Phe Val Val Ile Ser Ala Ser Phe Leu Tyr Met Val  
 1 5 10 15

Ser Leu Ser Met Lys Pro Tyr Gln Thr Ala Lys Ser Glu Gly Glu Lys  
 20 25 30

55 Leu Ala Gln Gln Tyr Ala Gly Leu Glu Gln Ala Asp Gln Val Asp Leu  
 35 40 45

Tyr Asn Gly Leu Glu Ser Tyr Tyr Ser Val Leu Gly Arg Asn Lys Gln  
 50 55 60  
 5 Gln Glu Ala Leu Ala Val Leu Ile Gly Lys Asp Asp His Lys Ile Tyr  
 65 70 75 80  
 Val Tyr Gln Leu Asn Gln Gly Val Ser Gln Glu Lys Ala Glu Thr Val  
 85 90 95  
 10 Ser Lys Glu Lys Gly Ala Gly Glu Ile Asp Lys Ile Ile Phe Gly Arg  
 100 105 110  
 Tyr Gln Asp Lys Pro Ile Trp Glu Val Lys Ser Gly Ser Asp Phe Tyr  
 115 120 125  
 15 Leu Val Asp Phe Glu Thr Gly Ala Leu Val Asn Lys Glu Gly Leu  
 130 135 140  
 20 <210> 186  
 <211> 243  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 25 <400> 186  
 Met Ile Asp Ile His Ser His Ile Val Phe Asp Val Asp Asp Gly Pro  
 1 5 10 15  
 30 Lys Ser Arg Glu Glu Ser Lys Ala Leu Leu Thr Glu Ala Tyr Arg Gln  
 20 25 30  
 Gly Val Arg Thr Ile Val Ser Thr Ser His Arg Arg Lys Gly Met Phe  
 35 40 45  
 35 Glu Thr Pro Glu Glu Lys Ile Ala Glu Asn Phe Leu Gln Val Arg Glu  
 50 55 60  
 Ile Ala Lys Glu Val Ala Ser Asp Leu Val Ile Ala Tyr Gly Ala Glu  
 65 70 75 80  
 40 Ile Tyr Tyr Thr Pro Asp Val Leu Asp Lys Leu Glu Asn Asn Arg Ile  
 85 90 95  
 Pro Thr Leu Asn Asn Ser Arg Tyr Ala Leu Ile Glu Phe Ser Met Asn  
 100 105 110  
 45 Thr Pro Tyr Arg Asp Ile His Ser Ala Leu Asn Lys Ile Leu Met Leu  
 115 120 125  
 50 Gly Ile Thr Pro Val Ile Ala His Ile Glu Arg Tyr Asp Val Leu Glu  
 130 135 140  
 Asn Asn Glu Lys Arg Val Arg Glu Leu Ile Asp Met Gly Cys Tyr Thr  
 145 150 155 160  
 55 Gln Ile Asn Ser Ser His Val Leu Lys Ser Lys Leu Phe Gly Glu Pro  
 165 170 175

Tyr Lys Phe Met Lys Lys Arg Ala Gln Tyr Phe Leu Glu Arg Asp Leu  
 180 185 190  
 5 Val His Ile Ile Ala Ser Asp Met His Asn Val Asp Gly Arg Pro Pro  
 195 200 205  
 His Met Ala Glu Ala Tyr Asp Leu Val Ser Gln Lys Tyr Gly Glu Ala  
 210 215 220  
 10 Lys Ala Gln Glu Leu Phe Ile Asp Asn Pro Arg Lys Ile Val Met Asp  
 225 230 235 240  
 Gln Leu Ile  
 15  
 <210> 187  
 <211> 308  
 20 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 187  
 25 Met Ser Thr Ile Asp Lys Glu Lys Phe Gln Phe Val Lys Arg Asp Asp  
 1 5 10 15  
 Phe Ala Ser Glu Thr Ile Asp Ala Pro Ala Tyr Ser Tyr Trp Lys Ser  
 20 25 30  
 30 Val Phe Lys Gln Phe Met Lys Lys Lys Ser Thr Val Val Met Leu Gly  
 35 40 45  
 Ile Leu Val Ala Ile Ile Leu Ile Ser Phe Ile Tyr Pro Met Phe Ser  
 50 55 60  
 35 Lys Phe Asp Phe Asn Asp Val Ser Lys Val Asn Asp Phe Ser Val Arg  
 65 70 75 80  
 40 Tyr Ile Lys Pro Asn Ala Glu His Trp Phe Gly Thr Asp Ser Asn Gly  
 85 90 95  
 Lys Ser Leu Phe Asp Gly Val Trp Phe Gly Ala Arg Asn Ser Ile Leu  
 100 105 110  
 45 Ile Ser Val Ile Ala Thr Val Ile Asn Leu Val Ile Gly Val Phe Val  
 115 120 125  
 Gly Gly Ile Trp Gly Ile Ser Lys Ser Val Asp Arg Val Met Met Glu  
 130 135 140  
 50 Val Tyr Asn Val Ile Ser Asn Ile Pro Pro Leu Leu Ile Val Ile Val  
 145 150 155 160  
 55 Leu Thr Tyr Ser Ile Gly Ala Gly Phe Trp Asn Leu Ile Phe Ala Met  
 165 170 175  
 Ser Val Thr Thr Trp Ile Gly Ile Ala Phe Met Ile Arg Val Gln Ile

180 185 190  
 Leu Arg Tyr Arg Asp Leu Glu Tyr Asn Leu Ala Ser Arg Thr Leu Gly  
 195 200 205  
 5 Thr Pro Thr Leu Lys Ile Val Ala Lys Asn Ile Met Pro Gln Leu Val  
 210 215 220  
 10 Ser Val Ile Val Thr Thr Met Thr Gln Met Leu Pro Ser Phe Ile Ser  
 225 230 235 240  
 Tyr Glu Ala Phe Leu Ser Phe Phe Gly Leu Gly Leu Pro Ile Thr Val  
 245 250 255  
 15 Pro Ser Leu Gly Arg Leu Ile Ser Asp Tyr Ser Gln Asn Val Thr Thr  
 260 265 270  
 Asn Ala Tyr Leu Phe Trp Ile Pro Leu Thr Thr Leu Val Leu Val Ser  
 275 280 285  
 20 Leu Ser Leu Phe Val Val Gly Gln Asn Leu Ala Asp Ala Ser Asp Pro  
 290 295 300  
 Arg Thr His Arg  
 25 305  
 <210> 188  
 <211> 77  
 30 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 188  
 Met Tyr Asn Leu Leu Leu Thr Ile Leu Leu Val Leu Ser Val Val Ile  
 35 1 5 10 15  
 Val Ile Ala Ile Phe Met Gln Pro Thr Lys Asn Gln Ser Ser Asn Val  
 20 25 30  
 40 Phe Asp Ala Ser Ser Gly Asp Leu Phe Glu Arg Ser Lys Ala Arg Gly  
 35 40 45  
 Phe Glu Ala Val Met Gln Arg Leu Thr Gly Ile Leu Val Phe Phe Trp  
 50 55 60  
 45 Leu Ala Ile Ala Leu Ala Leu Thr Val Leu Ser Ser Arg  
 65 70 75  
 50 <210> 189  
 <211> 369  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 55 <400> 189  
 Met Phe Arg Arg Asn Lys Leu Phe Phe Trp Thr Thr Glu Ile Leu Leu  
 1 5 10 15

Leu Thr Ile Ile Phe Tyr Leu Trp Arg Gln Met Gly Ser Leu Ile Asn  
 20 25 30  
 5 Pro Phe Val Ser Val Leu Asn Thr Ile Met Ile Pro Phe Leu Leu Gly  
 35 40 45  
 Gly Phe Leu Tyr Tyr Leu Thr Asn Pro Ile Val Thr Phe Leu Asn Lys  
 50 55 60  
 10 Val Cys Lys Leu Asn Arg Leu Leu Gly Ile Leu Ile Thr Leu Cys Thr  
 65 70 75 80  
 15 Leu Val Trp Gly Met Val Ile Gly Val Val Tyr Leu Leu Pro Ile Leu  
 85 90 95  
 Ile Asn Gln Leu Ser Ser Leu Ile Ile Ser Ser Gln Thr Ile Tyr Ser  
 100 105 110  
 20 Arg Val Gln Asp Leu Ile Ile Asp Leu Ser Asn Tyr Pro Ala Leu Gln  
 115 120 125  
 Asn Leu Asp Val Glu Ala Thr Ile Gln Gln Leu Asn Leu Ser Tyr Val  
 130 135 140  
 25 Asp Ile Leu Gln Asn Ile Leu Asn Ser Val Ser Asn Ser Val Gly Ser  
 145 150 155 160  
 30 Val Leu Ser Ala Leu Ile Ser Thr Val Leu Ile Leu Ile Met Thr Pro  
 165 170 175  
 Val Phe Leu Val Tyr Phe Leu Leu Asp Gly His Lys Phe Leu Pro Met  
 180 185 190  
 35 Leu Glu Arg Thr Ile Leu Lys Arg Asp Arg Leu His Ile Ala Gly Leu  
 195 200 205  
 Leu Lys Asn Leu Asn Ala Thr Ile Ala Arg Tyr Ile Ser Gly Val Ser  
 210 215 220  
 40 Ile Asp Ala Ile Ile Ile Gly Cys Leu Ala Tyr Ile Gly Tyr Ser Ile  
 225 230 235 240  
 45 Ile Gly Leu Lys Tyr Ala Leu Val Phe Ala Ile Phe Ser Gly Val Ala  
 245 250 255  
 Asn Leu Ile Pro Tyr Val Gly Pro Ser Ile Gly Leu Ile Pro Met Ile  
 260 265 270  
 50 Ile Ala Asn Ile Phe Thr Val Pro His Arg Leu Leu Ile Ala Val Ile  
 275 280 285  
 Tyr Met Leu Val Val Gln Gln Val Asp Gly Asn Ile Leu Tyr Pro Arg  
 290 295 300  
 55 Ile Val Gly Ser Val Met Lys Val His Pro Ile Thr Ile Leu Val Leu  
 305 310 315 320

Leu Leu Leu Ser Ser Asn Ile Tyr Gly Val Val Gly Met Ile Val Ala  
 325 330 335

5 Val Pro Thr Tyr Ser Ile Leu Lys Glu Ile Ser Lys Phe Leu Ser Arg  
 340 345 350

Leu Tyr Glu Asn His Lys Ile Met Lys Glu Arg Glu Arg Glu Leu Ala  
 355 360 365

10 Lys

15 <210> 190  
 <211> 451  
 <212> PRT  
 <213> Streptococcus pneumoniae

20 <400> 190  
 Met Tyr Gln Ala Leu Tyr Arg Lys Tyr Arg Ser Gln Asn Phe Ser Gln  
 1 5 10 15

25 Leu Val Gly Gln Glu Val Val Ala Lys Thr Leu Lys Gln Ala Val Glu  
 20 25 30

Gln Glu Lys Ile Ser His Ala Tyr Leu Phe Ser Gly Pro Arg Gly Thr  
 35 40 45

30 Gly Lys Thr Ser Val Ala Lys Ile Phe Ala Lys Ala Met Asn Cys Pro  
 50 55 60

Asn Gln Val Gly Gly Glu Pro Cys Asn Asn Cys Tyr Ile Cys Gln Ala  
 65 70 75 80

35 Val Thr Asp Gly Ser Leu Glu Asp Val Ile Glu Met Asp Ala Ala Ser  
 85 90 95

40 Asn Asn Gly Val Asp Glu Ile Arg Glu Ile Arg Asp Lys Ser Thr Tyr  
 100 105 110

Ala Pro Ser Leu Ala Arg Tyr Lys Val Tyr Ile Ile Asp Glu Val His  
 115 120 125

45 Met Leu Ser Thr Gly Ala Phe Asn Ala Leu Leu Lys Thr Leu Glu Glu  
 130 135 140

Pro Thr Gln Asn Val Val Phe Ile Leu Ala Thr Thr Glu Leu His Lys  
 145 150 155 160

50 Ile Pro Ala Thr Ile Leu Ser Arg Val Gln Arg Phe Glu Phe Lys Ser  
 165 170 175

55 Ile Lys Thr Gln Asp Ile Lys Glu His Ile His Tyr Ile Leu Glu Lys  
 180 185 190

Glu Asn Ile Ser Ser Glu Pro Glu Ala Val Glu Ile Ile Ala Arg Arg

|    | 195   | 200 | 205     |
|----|---|-----|---------|
|    | Ala Glu Gly Gly Met Arg Asp Ala Leu Ser Ile Leu Asp Gln Ala Leu |     |         |
|    | 210   | 215 | 220     |
| 5  | Ser Leu Thr Gln Gly Asn Glu Leu Thr Thr Ala Ile Ser Glu Glu Ile |     |         |
|    | 225   | 230 | 235 240 |
|    | Thr Gly Thr Ile Ser Leu Ser Ala Leu Asp Asp Tyr Val Ala Ala Leu |     |         |
| 10 |   | 245 | 250 255 |
|    | Ser Gln Gln Asp Val Pro Lys Ala Leu Ser Cys Leu Asn Leu Leu Phe |     |         |
|    | 260   | 265 | 270     |
| 15 | Asp Asn Gly Lys Ser Met Thr Arg Phe Val Thr Asp Leu Leu His Tyr |     |         |
|    | 275   | 280 | 285     |
|    | Leu Arg Asp Leu Leu Ile Val Gln Thr Gly Gly Glu Asn Thr His His |     |         |
| 20 |   | 295 | 300     |
|    | Ser Ser Val Phe Val Glu Asn Leu Ala Leu Pro Gln Lys Asn Leu Phe |     |         |
|    | 305   | 310 | 315 320 |
| 25 | Glu Met Ile Arg Leu Ala Thr Val Asn Leu Ala Asp Ile Lys Ser Ser |     |         |
|    | 325   | 330 | 335     |
|    | Leu Gln Pro Lys Ile Tyr Ala Glu Met Met Thr Val Arg Leu Ala Glu |     |         |
|    | 340   | 345 | 350     |
| 30 | Ile Lys Pro Glu Pro Ala Leu Ser Gly Ala Val Glu Asn Glu Ile Ala |     |         |
|    | 355   | 360 | 365     |
|    | Thr Leu Arg Gln Glu Val Ala Arg Leu Lys Gln Glu Leu Ser Asn Ala |     |         |
| 35 |   | 375 | 380     |
|    | Gly Ala Val Pro Lys Gln Val Ala Pro Ala Pro Ser Arg Pro Ala Thr |     |         |
|    | 385   | 390 | 395 400 |
| 40 | Gly Lys Thr Val Tyr Arg Val Asp Arg Asn Lys Val Gln Ser Ile Leu |     |         |
|    | 405   | 410 | 415     |
|    | Gln Glu Ala Val Glu Asn Pro Asp Leu Thr Arg Gln Asn Leu Ile Arg |     |         |
|    | 420   | 425 | 430     |
| 45 | Leu Gln Asn Ala Trp Gly Glu Val Ile Glu Ser Leu Gly Gly Pro Asp |     |         |
|    | 435   | 440 | 445     |
|    | Lys Leu Cys   |     |         |
| 50 | 450   |     |         |
|    | <210> 191   |     |         |
|    | <211> 662   |     |         |
|    | <212> PRT   |     |         |
| 55 | <213> Streptococcus pneumoniae                                  |     |         |
|    | <400> 191   |     |         |

Met Phe Arg Leu Thr Asn Lys Leu Ala Val Ser Asn Leu Ile Lys Asn  
 1 5 10 15  
 5 Arg Lys Leu Tyr Tyr Pro Phe Ala Leu Ala Val Leu Leu Ala Val Thr  
 20 25 30  
 Leu Thr Tyr Leu Phe Tyr Ser Leu Thr Phe Asn Pro Lys Ile Ala Glu  
 35 40 45  
 10 Ile Arg Gly Gly Thr Thr Ile Gln Ala Thr Leu Gly Phe Gly Met Phe  
 50 55 60  
 Val Val Thr Leu Ala Ser Ala Ile Ile Val Leu Tyr Ala Asn Ser Phe  
 65 70 75 80  
 15 Val Met Lys Lys Arg Ser Lys Glu Leu Gly Ile Tyr Gly Met Leu Gly  
 85 90 95  
 20 Leu Glu Lys Arg His Leu Ile Ser Met Thr Phe Lys Glu Leu Val Val  
 100 105 110  
 Phe Gly Ile Leu Thr Val Gly Ala Gly Ile Gly Ile Gly Ala Leu Phe  
 115 120 125  
 25 Asp Lys Leu Ile Phe Ala Phe Leu Leu Lys Leu Met Lys Leu Lys Val  
 130 135 140  
 Glu Leu Val Ala Thr Phe Gln Thr Lys Val Val Ile Thr Val Leu Val  
 145 150 155 160  
 30 Val Phe Gly Leu Ile Phe Leu Gly Leu Met Phe Leu Asn Ala Leu Arg  
 165 170 175  
 35 Ile Ala Arg Met Asn Ala Leu Gln Leu Ser Arg Glu Lys Ala Ser Gly  
 180 185 190  
 Glu Lys Lys Gly Arg Phe Leu Pro Leu Gln Thr Ile Leu Gly Ser Ile  
 195 200 205  
 40 Ser Leu Gly Ile Gly Tyr Tyr Leu Ala Leu Thr Val Lys Asp Pro Leu  
 210 215 220  
 Thr Ala Leu Thr Thr Phe Phe Ile Ala Val Leu Leu Val Ile Phe Gly  
 225 230 235 240  
 45 Thr Tyr Leu Leu Phe Asn Ala Gly Ile Thr Val Phe Leu Gln Ile Leu  
 245 250 255  
 50 Lys Lys Asn Lys Lys Tyr Tyr Tyr Gln Pro Asn Asn Leu Ile Ser Val  
 260 265 270  
 Ser Asn Leu Ile Phe Arg Met Lys Lys Asn Ala Val Gly Leu Ala Thr  
 275 280 285  
 55 Ile Ala Ile Leu Ser Thr Met Val Leu Val Thr Met Ser Ala Ala Thr  
 290 295 300



Ser Ile Phe Asn Ser Ala Glu Ser Phe Lys Lys Val Leu Asn Pro His  
 305 310 315 320  
 5 Asp Phe Gly Val Ser Gly Gln Asn Val Glu Lys Glu Asp Leu Asp Lys  
 325 330 335  
 Leu Leu Ser Gln Phe Ala Ser Asp Asn Gly Tyr Lys Ile Lys Glu Lys  
 340 345 350  
 10 Glu Val Phe Arg Tyr Thr Tyr Phe Gly Val Ala Asn Gln Glu Gly Asn  
 355 360 365  
 Lys Leu Thr Phe Phe Glu Lys Gly Gln Asn Arg Val Gln Pro Thr Thr  
 370 375 380  
 15 Val Phe Met Val Phe Asp Gln Lys Asp Tyr Glu Asn Met Thr Gly Gln  
 385 390 395 400  
 Lys Leu Ser Leu Ser Gly Asn Glu Val Gly Leu Phe Ala Lys Asn Asp  
 405 410 415  
 Gly Leu Lys Gly Gln Lys Thr Leu Ile Leu Asn Asp His Gln Phe Ser  
 420 425 430  
 25 Val Lys Glu Glu Phe Asn Lys Asp Phe Ile Val Asn His Val Pro Asn  
 435 440 445  
 Gln Phe Asn Ile Leu Thr Ala Asp Tyr Asn Tyr Leu Val Val Pro Asp  
 450 455 460  
 30 Leu Gln Ala Phe Leu Asn Gln Phe Pro Asp Ser Asp Ile Tyr Asn Gln  
 465 470 475 480  
 Phe Tyr Gly Gly Met Asn Val Asn Val Ser Glu Glu Glu Gln Leu Lys  
 485 490 495  
 Val Ala Glu Glu Tyr Glu Asn Tyr Leu Asn Gln Phe Asn Ala Gln Leu  
 500 505 510  
 40 Asp Thr Glu Gly Ser Tyr Val Tyr Gly Ser Asn Leu Ala Asp Ala Ser  
 515 520 525  
 Ser Gln Met Ser Ala Leu Phe Gly Gly Val Phe Phe Ile Gly Ile Phe  
 530 535 540  
 45 Leu Ser Ile Ile Phe Met Val Gly Thr Val Leu Val Ile Tyr Tyr Lys  
 545 550 555 560  
 Gln Ile Ser Glu Gly Tyr Glu Asp Arg Glu Arg Phe Ile Ile Leu Gln  
 565 570 575  
 Lys Val Gly Leu Asp Gln Lys Gln Ile Lys Gln Thr Ile His Lys Gln  
 580 585 590  
 55 Val Leu Thr Val Phe Phe Leu Pro Leu Leu Phe Ala Phe Ile His Leu  
 595 600 605

Ala Phe Ala Tyr His Met Leu Ser Leu Ile Leu Lys Val Ile Gly Val  
610 615 620

5 Leu Asp Thr Thr Met Met Leu Ile Val Thr Leu Ser Ile Cys Ala Ile  
625 630 635 640

Phe Leu Ile Ala Tyr Val Leu Ile Phe Met Ile Thr Ser Arg Ser Tyr  
645 650 655

10 Arg Lys Ile Val Gln Met  
660

15 <210> 192  
<211> 296  
<212> PRT  
<213> Streptococcus pneumoniae

20 <400> 192  
Met Lys Gln Asp Gln Leu Lys Ala Trp Gln Pro Ala Gln Phe Asp Arg  
1 5 10 15

Phe Val Arg Ile Leu Glu Gln Asp Gln Leu Asn His Ala Tyr Leu Phe  
20 25 30

25 Ser Gly Phe Phe Gly Ser Leu Glu Met Ala Gln Phe Leu Ala Lys Ser  
35 40 45

30 Leu Phe Cys Thr Asp Lys Val Gly Val Leu Pro Cys Glu Lys Cys Arg  
50 55 60

Ser Cys Lys Leu Ile Glu Gln Glu Glu Phe Pro Asp Val Thr Leu Ile  
65 70 75 80

35 Lys Pro Val Asn Gln Val Ile Lys Thr Glu Arg Ile Arg Glu Leu Val  
85 90 95

Gly Gln Phe Ser Gln Ala Gly Ile Glu Ser Gln Gln Gln Val Phe Ile  
100 105 110

40 Ile Glu Gln Ala Asp Lys Met His Pro Asn Ala Ala Asn Ser Leu Leu  
115 120 125

45 Lys Val Ile Glu Glu Pro Gln Ser Glu Val Tyr Ile Phe Phe Leu Thr  
130 135 140

Ser Asp Glu Glu Lys Met Leu Pro Thr Ile Arg Ser Arg Thr Gln Ile  
145 150 155 160

50 Phe His Phe Lys Lys Gln Glu Glu Lys Leu Ile Leu Leu Leu Glu Gln  
165 170 175

Met Gly Leu Val Lys Lys Lys Ala Thr Leu Leu Ala Lys Phe Ser Gln  
180 185 190

55 Ser Arg Ala Glu Ala Glu Lys Leu Ala Asn Gln Ala Ser Phe Trp Thr  
195 200 205

Leu Val Asp Glu Ser Glu Arg Leu Leu Thr Trp Leu Val Ala Lys Lys  
 210 215 220  
 5 Lys Glu Ser Tyr Leu Gln Val Ala Lys Leu Ala Asn Leu Ala Asp Asp  
 225 230 235 240  
 Lys Glu Lys Gln Asp Gln Val Leu Arg Ile Leu Glu Val Leu Cys Gly  
 245 250 255  
 10 Gln Asp Leu Leu Gln Val Arg Val Arg Val Ile Leu Gln Asp Leu Leu  
 260 265 270  
 Glu Ala Arg Lys Met Trp Gln Ala Asn Val Ser Phe Gln Asn Ala Met  
 15 275 280 285  
 Glu Tyr Leu Val Leu Lys Glu Ile  
 290 295  
 20  
 <210> 193  
 <211> 204  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 25  
 <400> 193  
 Met Asn Ser Phe Lys Asn Phe Leu Lys Glu Trp Gly Leu Phe Leu Leu  
 1 5 10 15  
 30 Ile Leu Ser Leu Leu Ala Leu Ser Arg Ile Phe Phe Trp Ser Asn Val  
 20 25 30  
 Arg Val Glu Gly His Ser Met Asp Pro Thr Leu Ala Asp Gly Glu Ile  
 35 35 40 45  
 Leu Phe Val Val Lys His Leu Pro Ile Asp Arg Phe Asp Ile Val Val  
 50 55 60  
 40 Ala His Glu Glu Asp Gly Asn Lys Asp Ile Val Lys Arg Val Ile Gly  
 65 70 75 80  
 Met Pro Gly Asp Thr Ile Arg Tyr Glu Asn Asp Lys Leu Tyr Ile Asn  
 85 90 95  
 45 Asp Lys Glu Thr Asp Glu Pro Tyr Leu Ala Asp Tyr Ile Lys Arg Phe  
 100 105 110  
 Lys Asp Asp Lys Leu Gln Ser Thr Tyr Ser Gly Lys Gly Phe Glu Gly  
 115 120 125  
 50 Asn Lys Gly Thr Phe Phe Arg Ser Ile Ala Gln Lys Ala Gln Ala Phe  
 130 135 140  
 55 Thr Val Asp Val Asn Tyr Asn Thr Asn Phe Ser Phe Thr Val Pro Glu  
 145 150 155 160  
 Gly Glu Tyr Leu Leu Leu Gly Asp Asp Arg Leu Val Ser Ser Asp Ser

165 170 175  
 Arg His Val Gly Thr Phe Lys Ala Lys Asp Ile Thr Gly Glu Ala Lys  
 180 185 190  
 5 Phe Arg Phe Trp Pro Ile Thr Arg Ile Gly Thr Phe  
 195 200  
 10 <210> 194  
 <211> 328  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 15 <400> 194  
 Met Val Val Phe Thr Gly Ser Thr Val Glu Glu Ala Ile Gln Lys Gly  
 1 5 10 15  
 20 Leu Lys Glu Leu Asp Ile Pro Arg Met Lys Ala His Ile Lys Val Ile  
 20 25 30  
 Ser Arg Glu Lys Lys Gly Phe Leu Gly Leu Phe Gly Lys Lys Pro Ala  
 35 40 45  
 25 Gln Val Asp Ile Glu Ala Ile Ser Glu Thr Thr Val Val Lys Ala Asn  
 50 55 60  
 Gln Gln Val Val Lys Gly Val Pro Lys Lys Ile Asn Asp Leu Asn Glu  
 65 70 75 80  
 30 Pro Val Lys Thr Val Ser Glu Glu Thr Val Asp Leu Gly His Val Val  
 85 90 95  
 35 Asn Ala Ile Lys Lys Ile Glu Glu Glu Gly Gln Gly Ile Ser Asp Glu  
 100 105 110  
 Val Lys Ala Glu Ile Leu Lys His Glu Arg His Ala Ser Thr Ile Leu  
 115 120 125  
 40 Glu Glu Thr Gly His Ile Glu Ile Leu Asn Glu Leu Gln Ile Glu Glu  
 130 135 140  
 Ala Met Arg Glu Glu Ala Gly Ala Asp Asp Leu Glu Thr Glu Gln Asp  
 145 150 155 160  
 45 Gln Thr Glu Asn Gln Asp Leu Lys Glu Met Gly Leu Lys Val Glu Gln  
 165 170 175  
 50 Ser Tyr Asp Ile Ala Gln Val Ala Thr Asp Val Thr Ala Tyr Val Gln  
 180 185 190  
 Ala Ile Val Asp Asp Met Asp Val Glu Ala Thr Leu Ser Asn Asp Tyr  
 195 200 205  
 55 Asn Arg Arg Ser Ile Asn Leu Gln Ile Asp Thr Asn Glu Pro Gly Arg  
 210 215 220

Ile Ile Gly Tyr His Gly Lys Val Leu Lys Ala Leu Gln Leu Leu Ala  
 225 230 235 240  
 5 Gln Asn Tyr Leu Tyr Asn Arg Tyr Ser Lys Thr Phe Tyr Val Thr Ile  
 245 250 255  
 Asn Val Asn Asp Tyr Val Glu His Arg Ala Glu Val Leu Gln Thr Tyr  
 260 265 270  
 10 Ala Gln Lys Leu Ala Asn Arg Val Leu Glu Glu Gly Arg Ser His Lys  
 275 280 285  
 Thr Asp Pro Met Ser Asn Ser Glu Arg Lys Ile Ile His Arg Ile Ile  
 290 295 300  
 15 Ser Arg Met Asp Gly Val Thr Ser Tyr Ser Glu Gly Asp Glu Pro Asn  
 305 310 315 320  
 20 Arg Tyr Val Val Val Asp Thr Glu  
 325  
 <210> 195  
 <211> 460  
 25 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 195  
 30 Met Ser Asn Phe Ala Ile Ile Leu Ala Ala Gly Lys Gly Thr Arg Met  
 1 5 10 15  
 Lys Ser Asp Leu Pro Lys Val Leu His Lys Val Ala Gly Ile Ser Met  
 20 25 30  
 35 Leu Glu His Val Phe Arg Ser Val Gly Ala Ile Gln Pro Glu Lys Thr  
 35 40 45  
 Val Thr Val Val Gly His Lys Ala Glu Leu Val Glu Glu Val Leu Ala  
 50 55 60  
 40 Gly Gln Thr Glu Phe Val Thr Gln Ser Glu Gln Leu Gly Thr Gly His  
 65 70 75 80  
 45 Ala Val Met Met Thr Glu Pro Ile Leu Glu Gly Val Ser Gly His Thr  
 85 90 95  
 Leu Val Ile Ala Gly Asp Thr Pro Leu Ile Thr Gly Glu Ser Leu Lys  
 100 105 110  
 50 Asn Leu Ile Asp Phe His Ile Asn His Lys Asn Val Ala Thr Ile Leu  
 115 120 125  
 Thr Ala Glu Thr Asp Asn Pro Phe Gly Tyr Gly Arg Ile Val Arg Asn  
 130 135 140  
 55 Asp Asn Ala Glu Val Leu Arg Ser Leu Leu Ser Arg Arg Met Leu Gln  
 145 150 155 160

Ile Leu Lys Ser Lys Ser Arg Lys Ser Thr Leu Val Thr Tyr Val Phe  
 165 170 175  
 5 Asp Asn Glu Arg Leu Phe Glu Ala Leu Lys Asn Ile Asn Thr Asn Asn  
 180 185 190  
 Ala Gln Gly Glu Tyr Tyr Ile Thr Asp Val Ile Gly Ile Phe Arg Glu  
 195 200 205  
 10 Thr Gly Glu Lys Val Gly Ala Tyr Thr Leu Lys Asp Phe Asp Glu Ser  
 210 215 220  
 Leu Gly Val Asn Asp Arg Val Ala Leu Ala Thr Ala Glu Ser Val Met  
 15 225 230 235 240  
 Arg Arg Arg Ile Asn His Lys His Met Val Asn Gly Val Ser Phe Val  
 245 250 255  
 20 Asn Pro Glu Ala Thr Tyr Ile Asp Ile Asp Val Glu Ile Ala Pro Glu  
 260 265 270  
 Val Gln Ile Glu Ala Asn Val Ile Leu Lys Gly Gln Thr Lys Ile Gly  
 275 280 285  
 25 Ala Glu Thr Val Leu Thr Asn Gly Thr Tyr Val Val Asp Ser Thr Ile  
 290 295 300  
 Gly Ala Gly Ala Val Ile Thr Asn Ser Met Ile Glu Glu Ser Ser Val  
 30 305 310 315 320  
 Ala Asp Gly Val Thr Val Gly Pro Tyr Ala His Ile Arg Pro Asn Ser  
 325 330 335  
 35 Ser Leu Gly Ala Gln Val His Ile Gly Asn Phe Val Glu Val Lys Gly  
 340 345 350  
 Ser Ser Ile Gly Glu Asn Thr Lys Ala Gly His Leu Thr Tyr Ile Gly  
 355 360 365  
 40 Asn Cys Glu Val Gly Ser Asn Val Asn Phe Gly Ala Gly Thr Ile Thr  
 370 375 380  
 Val Asn Tyr Asp Gly Lys Asn Lys Tyr Lys Thr Val Ile Gly Val Asn  
 45 385 390 395 400  
 Val Phe Val Gly Ser Asn Ser Thr Ile Ile Ala Pro Val Glu Leu Gly  
 405 410 415  
 50 Asp Asn Ser Leu Val Gly Ala Gly Ser Thr Ile Thr Lys Asp Val Pro  
 420 425 430  
 Ala Asp Ala Ile Ala Ile Gly Arg Gly Arg Gln Ile Asn Lys Asp Glu  
 435 440 445  
 55 Tyr Ala Thr Arg Leu Pro His His Pro Lys Asn Gln  
 450 455 460

<210> 196  
 <211> 311  
 5 <212> PRT  
 <213> Streptococcus pneumoniae  
  
 <400> 196  
 10 Met Ser Lys Ile Leu Val Phe Gly His Gln Asn Pro Asp Ser Asp Ala  
     1                    5                    10                    15  
     Ile Gly Ser Ser Val Ala Phe Ala Tyr Leu Ala Lys Glu Ala Tyr Gly  
                     20                    25                    30  
 15 Leu Asp Thr Glu Ala Val Ala Leu Gly Thr Pro Asn Glu Glu Thr Ala  
             35                    40                    45  
     Phe Val Leu Asn Tyr Phe Gly Val Glu Ala Pro Arg Val Ile Thr Ser  
             50                    55                    60  
 20 Ala Lys Ala Glu Gly Ala Glu Gln Val Ile Leu Thr Asp His Asn Glu  
     65                    70                    75                    80  
     Phe Gln Gln Ser Val Ser Asp Ile Ala Glu Val Glu Val Tyr Gly Val  
 25                    85                    90                    95  
     Val Asp His His Arg Val Ala Asn Phe Glu Thr Ala Ser Pro Leu Tyr  
             100                    105                    110  
 30 Met Arg Leu Glu Pro Val Gly Ser Ala Ser Ser Ile Val Tyr Arg Met  
             115                    120                    125  
     Phe Lys Glu His Gly Val Ala Val Pro Lys Glu Ile Ala Gly Leu Met  
             130                    135                    140  
 35 Leu Ser Gly Leu Ile Ser Asp Thr Leu Leu Leu Lys Ser Pro Thr Thr  
     145                    150                    155                    160  
     His Pro Thr Asp Lys Ile Ile Ala Pro Glu Leu Ala Glu Leu Ala Gly  
 40                    165                    170                    175  
     Val Asn Leu Glu Glu Tyr Gly Leu Ala Met Leu Lys Ala Gly Thr Asn  
             180                    185                    190  
 45 Leu Ala Ser Lys Ser Ala Glu Glu Leu Ile Asp Ile Asp Ala Lys Thr  
             195                    200                    205  
     Phe Glu Leu Asn Gly Asn Asn Val Arg Val Ala Gln Val Asn Thr Val  
             210                    215                    220  
 50 Asp Ile Ala Glu Val Leu Glu Arg Gln Ala Glu Ile Glu Ala Ala Met  
     225                    230                    235                    240  
     Gln Ala Ala Asn Glu Ser Asn Gly Tyr Ser Asp Phe Val Leu Met Ile  
 55                    245                    250                    255  
     Thr Asp Ile Val Asn Ser Asn Ser Glu Ile Leu Ala Leu Gly Ala Asn

260 265 270  
 Met Asp Lys Val Glu Ala Ala Phe Asn Phe Lys Leu Glu Asn Asn His  
 275 280 285  
 5 Ala Phe Leu Ala Gly Ala Val Ser Arg Lys Lys Gln Val Val Pro Gln  
 290 295 300  
 10 Leu Thr Glu Ser Phe Asn Thr  
 305 310  
 15 <210> 197  
 <211> 225  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 197  
 20 Met Ile Ser Lys Arg Leu Glu Leu Val Ala Ser Phe Val Ser Gln Gly  
 1 5 10 15  
 Ala Ile Leu Leu Asp Val Gly Ser Asp His Ala Tyr Leu Pro Ile Glu  
 20 25 30  
 25 Leu Val Glu Arg Gly Gln Ile Lys Ser Ala Ile Ala Gly Glu Val Val  
 35 40 45  
 Glu Gly Pro Tyr Gln Ser Ala Val Lys Asn Val Glu Ala His Gly Leu  
 50 55 60  
 30 Lys Glu Lys Ile Gln Val Arg Leu Ala Asn Gly Leu Ala Ala Phe Glu  
 65 70 75 80  
 35 Glu Thr Asp Gln Val Ser Val Ile Thr Ile Ala Gly Met Gly Gly Arg  
 85 90 95  
 Leu Ile Ala Arg Ile Leu Glu Glu Gly Leu Gly Lys Leu Ala Asn Val  
 100 105 110  
 40 Glu Arg Leu Ile Leu Gln Pro Asn Asn Arg Glu Asp Asp Leu Arg Ile  
 115 120 125  
 Trp Leu Gln Asp His Gly Phe Gln Ile Val Ala Glu Ser Ile Leu Glu  
 130 135 140  
 45 Glu Ala Gly Lys Phe Tyr Glu Ile Leu Val Val Glu Ala Gly Gln Met  
 145 150 155 160  
 50 Lys Leu Ser Ala Ser Asp Val Arg Phe Gly Pro Phe Leu Ser Lys Glu  
 165 170 175  
 Val Ser Pro Val Phe Val Gln Lys Trp Gln Lys Glu Ala Glu Lys Leu  
 180 185 190  
 55 Glu Phe Ala Leu Gly Gln Ile Pro Glu Lys Asn Leu Glu Glu Arg Gln  
 195 200 205



Val Leu Val Asp Lys Ile Gln Ala Ile Lys Glu Val Leu His Val Ser  
 210 215 220

Lys  
 5 225

<210> 198  
 <211> 161  
 10 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 198  
 Met Asn Leu Asn Asp Ile Lys Asp Leu Met Thr Gln Phe Asp Gln Ser  
 15 1 5 10 15

Ser Leu Arg Glu Phe Ser Tyr Lys Asn Gly Thr Asp Glu Leu Gln Phe  
 20 20 25 30

Ser Lys Asn Glu Ala Arg Pro Val Pro Glu Val Ala Thr Gln Val Ala  
 35 40 45

Pro Ala Pro Val Leu Ala Thr Pro Ser Pro Val Ala Pro Thr Ser Ala  
 50 55 60

25 Pro Ala Glu Thr Val Ala Glu Glu Val Pro Ala Pro Ala Glu Ala Ser  
 65 70 75 80

Val Ala Ser Glu Gly Asn Leu Val Glu Ser Pro Leu Val Gly Val Val  
 85 90 95

30 Tyr Leu Ala Ala Gly Pro Asp Lys Pro Ala Phe Val Thr Val Gly Asp  
 100 105 110

35 Ser Val Lys Lys Gly Gln Thr Leu Val Ile Ile Glu Ala Met Lys Val  
 115 120 125

Met Asn Glu Ile Pro Ala Pro Lys Asp Gly Val Val Thr Glu Ile Leu  
 130 135 140

40 Val Ser Asn Glu Glu Met Val Glu Phe Gly Lys Gly Leu Val Arg Ile  
 145 150 155 160

Lys  
 45

<210> 199  
 <211> 411  
 50 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 199  
 Met Lys Leu Asn Arg Val Val Val Thr Gly Tyr Gly Val Thr Ser Pro  
 55 1 5 10 15

Ile Gly Asn Thr Pro Glu Glu Phe Trp Asn Ser Leu Ala Thr Gly Lys

|    | 20  | 25  | 30  |
|----|---|-----|-----|
|    | Ile Gly Ile Gly Gly Ile Thr Lys Phe Asp His Ser Asp Phe Asp Val |     |     |
|    | 35  | 40  | 45  |
| 5  | His Asn Ala Ala Glu Ile Gln Asp Phe Pro Phe Asp Lys Tyr Phe Val |     |     |
|    | 50  | 55  | 60  |
| 10 | Lys Lys Asp Thr Asn Arg Phe Asp Asn Tyr Ser Leu Tyr Ala Leu Tyr |     |     |
|    | 65  | 70  | 75  |
|    | Ala Ala Gln Glu Ala Val Asn His Ala Asn Leu Asp Val Glu Ala Leu |     |     |
|    | 85  | 90  | 95  |
| 15 | Asn Arg Asp Arg Phe Gly Val Ile Val Ala Ser Gly Ile Gly Gly Ile |     |     |
|    | 100   | 105 | 110 |
|    | Lys Glu Ile Glu Asp Gln Val Leu Arg Leu His Glu Lys Gly Pro Lys |     |     |
|    | 115   | 120 | 125 |
| 20 | Arg Val Lys Pro Met Thr Leu Pro Lys Ala Leu Pro Asn Met Ala Ser |     |     |
|    | 130   | 135 | 140 |
|    | Gly Asn Val Ala Met Arg Phe Gly Ala Asn Gly Val Cys Lys Ser Ile |     |     |
| 25 | 145   | 150 | 155 |
|    | Asn Thr Ala Cys Ser Ser Ser Asn Asp Ala Ile Gly Asp Ala Phe Arg |     |     |
|    | 165   | 170 | 175 |
| 30 | Ser Ile Lys Phe Gly Phe Gln Asp Val Met Leu Val Gly Gly Thr Glu |     |     |
|    | 180   | 185 | 190 |
|    | Ala Ser Ile Thr Pro Phe Ala Ile Ala Gly Phe Gln Ala Leu Thr Ala |     |     |
|    | 195   | 200 | 205 |
| 35 | Leu Ser Thr Thr Glu Asp Pro Thr Arg Ala Ser Ile Pro Phe Asp Lys |     |     |
|    | 210   | 215 | 220 |
|    | Asp Arg Asn Gly Phe Val Met Gly Glu Gly Ser Gly Met Leu Val Leu |     |     |
| 40 | 225   | 230 | 235 |
|    | Glu Ser Leu Glu His Ala Glu Lys Arg Gly Ala Thr Ile Leu Ala Glu |     |     |
|    | 245   | 250 | 255 |
| 45 | Val Val Gly Tyr Gly Asn Thr Cys Asp Ala Tyr His Met Thr Ser Pro |     |     |
|    | 260   | 265 | 270 |
|    | His Pro Glu Gly Gln Gly Ala Ile Lys Ala Ile Lys Leu Ala Leu Glu |     |     |
|    | 275   | 280 | 285 |
| 50 | Glu Ala Glu Ile Ser Pro Glu Gln Val Ala Tyr Val Asn Ala His Gly |     |     |
|    | 290   | 295 | 300 |
|    | Thr Ser Thr Pro Ala Asn Glu Lys Gly Glu Ser Gly Ala Ile Val Ala |     |     |
| 55 | 305   | 310 | 315 |
|    | Val Leu Gly Lys Glu Val Pro Val Ser Ser Thr Lys Ser Phe Thr Gly |     |     |

145

Leu Lys Tyr Glu Ser Gly Ala His Arg Val Gln Arg Val Pro Val Thr  
 180 185 190  
 5 Glu Ser Gln Gly Arg Val His Thr Ser Thr Ala Thr Val Leu Val Met  
 195 200 205  
 Pro Glu Val Glu Glu Val Glu Tyr Asp Ile Asp Pro Lys Asp Leu Arg  
 210 215 220  
 10 Val Asp Ile Tyr His Ala Ser Gly Ala Gly Gly Gln Asn Val Asn Lys  
 225 230 235 240  
 Val Ala Thr Ala Val Arg Ile Val His Leu Pro Thr Asn Ile Lys Val  
 245 250 255  
 15 Glu Met Gln Glu Glu Arg Thr Gln Gln Lys Asn Arg Glu Lys Ala Met  
 260 265 270  
 Lys Ile Ile Arg Ala Arg Val Ala Asp His Phe Ala Gln Ile Ala Gln  
 275 280 285  
 20 Asp Glu Gln Asp Ala Glu Arg Lys Ser Thr Ile Gly Thr Gly Asp Arg  
 290 295 300  
 25 Ser Glu Arg Ile Arg Thr Tyr Asn Phe Pro Gln Asn Arg Val Thr Asp  
 305 310 315 320  
 His Arg Ile Gly Leu Thr Leu Gln Lys Leu Asp Thr Ile Leu Ser Gly  
 325 330 335  
 30 Lys Leu Asp Glu Val Val Asp Ala Leu Val Leu Tyr Asp Gln Thr Gln  
 340 345 350  
 Lys Leu Glu Glu Leu Asn Lys  
 35 355  
 <210> 201  
 <211> 559  
 40 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 201  
 Met Ala Tyr Thr Leu Lys Pro Glu Glu Val Gly Val Phe Ala Ile Gly  
 1 5 10 15  
 Gly Leu Gly Glu Ile Gly Lys Asn Thr Tyr Gly Ile Glu Tyr Gln Asp  
 20 25 30  
 50 Glu Ile Ile Ile Val Asp Ala Gly Ile Lys Phe Pro Glu Asp Asp Leu  
 35 40 45  
 Leu Gly Ile Asp Tyr Val Ile Pro Asp Tyr Ser Tyr Ile Val Asp Asn  
 50 55 60  
 55 Ile Asp Arg Val Lys Ala Val Leu Ile Thr His Gly His Glu Asp His  
 65 70 75 80

Ile Gly Gly Ile Pro Phe Leu Leu Lys Gln Ala Asn Val Pro Ile Tyr  
                                   85                                  90                                  95  
 5 Ala Gly Pro Leu Ala Leu Ala Leu Ile Arg Gly Lys Leu Glu Glu His  
                                   100                                  105                                  110  
 Gly Leu Leu Arg Asn Ala Lys Leu Tyr Glu Ile Asn His Asn Thr Glu  
                                   115                                  120                                  125  
 10 Leu Thr Phe Lys Asn Leu Lys Ala Thr Phe Phe Arg Thr Thr His Ser  
                                   130                                  135                                  140  
 Ile Pro Glu Pro Leu Gly Ile Val Ile His Thr Pro Gln Gly Lys Ile  
 15 145                                  150                                  155                                  160  
 Val Cys Thr Gly Asp Phe Lys Phe Asp Phe Thr Pro Val Gly Glu Pro  
                                   165                                  170                                  175  
 20 Ala Asp Leu His Arg Met Ala Ala Leu Gly Glu Glu Gly Val Leu Cys  
                                   180                                  185                                  190  
 Leu Leu Ser Asp Ser Thr Asn Ala Glu Val Pro Thr Phe Thr Asn Ser  
                                   195                                  200                                  205  
 25 Glu Lys Val Val Gly Gln Ser Ile Met Lys Ile Ile Gln Gly Ile Glu  
                                   210                                  215                                  220  
 Gly Arg Ile Ile Phe Ala Ser Phe Ala Ser Asn Ile Phe Arg Leu Gln  
 30 225                                  230                                  235                                  240  
 Gln Ala Thr Glu Ala Ala Val Lys Thr Gly Arg Lys Ile Ala Val Phe  
                                   245                                  250                                  255  
 35 Gly Arg Ser Met Glu Lys Ala Ile Val Asn Gly Ile Asp Leu Gly Tyr  
                                   260                                  265                                  270  
 Ile Lys Ala Pro Lys Gly Thr Phe Ile Glu Pro Asn Glu Ile Lys Asp  
                                   275                                  280                                  285  
 40 Tyr Pro Ala Gly Glu Val Leu Ile Leu Cys Thr Gly Ser Gln Gly Glu  
                                   290                                  295                                  300  
 Pro Met Ala Ala Leu Ser Arg Ile Ala Asn Gly Thr His Arg Gln Val  
 45 305                                  310                                  315                                  320  
 Gln Leu Gln Pro Gly Asp Thr Val Ile Phe Ser Ser Ser Pro Ile Pro  
                                   325                                  330                                  335  
 50 Gly Asn Thr Thr Ser Val Asn Lys Leu Ile Asn Ile Ile Ser Glu Ala  
                                   340                                  345                                  350  
 Gly Val Glu Val Ile His Gly Lys Val Asn Asn Ile His Thr Ser Gly  
                                   355                                  360                                  365  
 55 His Gly Gly Gln Gln Glu Gln Lys Leu Met Leu Cys Leu Ile Lys Pro  
                                   370                                  375                                  380

Lys Tyr Phe Met Pro Val His Gly Glu Tyr Arg Met Gln Lys Val His  
 385 390 395 400  
 5 Ala Gly Leu Ala Val Asp Thr Gly Val Glu Lys Asp Asn Ile Phe Ile  
 405 410 415  
 Met Ser Asn Gly Asp Val Leu Ala Leu Thr Ala Asp Ser Ala Arg Ile  
 420 425 430  
 10 Ala Gly His Phe Asn Ala Gln Asp Ile Tyr Val Asp Gly Asn Arg Ile  
 435 440 445  
 Gly Glu Ile Gly Ala Ala Val Leu Lys Asp Arg Arg Asp Leu Ser Glu  
 15 450 455 460  
 Asp Gly Val Val Leu Ala Val Ala Thr Val Asp Phe Lys Ser Gln Met  
 465 470 475 480  
 20 Ile Leu Ser Gly Pro Asp Ile Leu Ser Arg Gly Phe Val Tyr Met Arg  
 485 490 495  
 Glu Ser Gly Asp Leu Ile Arg Gln Ser Gln Arg Ile Leu Phe Asn Ala  
 500 505 510  
 25 Ile Arg Ile Ala Leu Lys Asn Lys Asp Ala Ser Val Gln Ser Val Asn  
 515 520 525  
 Gly Ala Ile Val Asn Ala Ile Arg Pro Phe Leu Tyr Glu Asn Thr Glu  
 30 530 535 540  
 Arg Glu Pro Ile Ile Ile Pro Met Ile Leu Thr Pro Asp Glu Glu  
 545 550 555  
 35  
 <210> 202  
 <211> 450  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 40  
 <400> 202  
 Met Ala Glu Val Glu Glu Leu Arg Val Gln Pro Gln Asp Ile Leu Ala  
 1 5 10 15  
 45 Glu Gln Ser Val Leu Gly Ala Ile Phe Ile Asp Glu Ser Lys Leu Val  
 20 25 30  
 Phe Val Arg Glu Tyr Ile Glu Ser Arg Asp Phe Phe Lys Tyr Ala His  
 35 40 45  
 50 Arg Leu Ile Phe Gln Ala Met Val Asp Leu Ser Asp Arg Gly Asp Ala  
 50 55 60  
 55 Ile Asp Ala Thr Thr Val Arg Thr Ile Leu Asp Asn Gln Gly Asp Leu  
 65 70 75 80  
 Gln Asn Ile Gly Gly Leu Ser Tyr Leu Val Glu Ile Val Asn Ser Val

|    | 85  | 90  | 95  |
|----|---|-----|-----|
|    | Pro Thr Ser Ala Asn Ala Glu Tyr Tyr Ala Lys Ile Val Ala Glu Lys |     |     |
|    | 100   | 105 | 110 |
| 5  | Ala Met Leu Arg Arg Leu Ile Ala Lys Leu Thr Glu Ser Val Asn Gln |     |     |
|    | 115   | 120 | 125 |
|    | Ala Tyr Glu Ala Ser Gln Pro Ala Asp Glu Ile Ile Ala Gln Ala Glu |     |     |
| 10 | 130   | 135 | 140 |
|    | Lys Gly Leu Ile Asp Val Ser Glu Asn Ala Asn Arg Ser Gly Phe Lys |     |     |
|    | 145   | 150 | 155 |
| 15 | Asn Ile Arg Asp Val Leu Asn Leu Asn Phe Gly Asn Leu Glu Ala Arg |     |     |
|    | 165   | 170 | 175 |
|    | Ser Gln Gln Thr Thr Asp Ile Thr Gly Ile Ala Thr Gly Tyr Arg Asp |     |     |
| 20 | 180   | 185 | 190 |
|    | Leu Asp His Met Thr Thr Gly Leu His Glu Glu Glu Leu Ile Ile Leu |     |     |
|    | 195   | 200 | 205 |
|    | Ala Ala Arg Pro Ala Val Gly Lys Thr Ala Phe Ala Leu Asn Ile Ala |     |     |
| 25 | 210   | 215 | 220 |
|    | Gln Asn Ile Gly Thr Lys Leu Asp Lys Thr Val Ala Ile Phe Ser Leu |     |     |
|    | 225   | 230 | 235 |
| 30 | Glu Met Gly Ala Glu Ser Leu Val Asp Arg Met Leu Ala Ala Glu Gly |     |     |
|    | 245   | 250 | 255 |
|    | Leu Val Glu Ser His Ser Ile Arg Thr Gly Gln Leu Thr Asp Glu Glu |     |     |
| 35 | 260   | 265 | 270 |
|    | Trp Gln Lys Tyr Thr Ile Ala Gln Gly Asn Leu Ala Asn Ala Ser Ile |     |     |
|    | 275   | 280 | 285 |
|    | Tyr Ile Asp Asp Thr Pro Gly Ile Arg Ile Thr Glu Ile Arg Ser Arg |     |     |
| 40 | 290   | 295 | 300 |
|    | Ser Arg Lys Leu Ala Gln Glu Thr Gly Asn Leu Gly Leu Ile Val Ile |     |     |
|    | 305   | 310 | 315 |
| 45 | Asp Tyr Leu Gln Leu Ile Thr Gly Thr Gly Arg Glu Asn Arg Gln Gln |     |     |
|    | 325   | 330 | 335 |
|    | Glu Val Ser Glu Ile Ser Arg Gln Leu Lys Ile Leu Ala Lys Glu Leu |     |     |
| 50 | 340   | 345 | 350 |
|    | Lys Val Pro Val Ile Ala Leu Ser Gln Leu Ser Arg Gly Val Glu Gln |     |     |
|    | 355   | 360 | 365 |
|    | Arg Gln Asp Lys Arg Pro Val Leu Ser Asp Ile Arg Glu Ser Gly Ser |     |     |
| 55 | 370   | 375 | 380 |
|    | Ile Glu Gln Asp Ala Asp Ile Val Ala Phe Leu Tyr Arg Asp Asp Tyr |     |     |

385                      390                      395                      400  
 Tyr Glu Arg Gly Gly Glu Glu Glu Glu Gly Ile Pro Asn Asn Lys Val  
                                  405                      410                      415  
 5    Glu Val Ile Ile Glu Lys Asn Arg Ser Gly Ala Arg Gly Thr Val Glu  
                                  420                      425                      430  
 10   Leu Ile Val Gln Lys Glu Tyr Asn Lys Phe Ser Ser Ile Ser Lys Arg  
                                  435                      440                      445  
      Glu Ala  
          450  
 15   <210> 203  
      <211> 699  
      <212> PRT  
      <213> Streptococcus pneumoniae  
 20   <400> 203  
      Met Ala Thr Ala Thr Lys Lys Lys Lys Ser Thr Val Lys Lys Asn Leu  
          1                      5                      10                      15  
 25   Val Ile Val Glu Ser Pro Ala Lys Ala Lys Thr Ile Glu Lys Tyr Leu  
                                  20                      25                      30  
      Gly Arg Asn Tyr Lys Val Leu Ala Ser Val Gly His Ile Arg Asp Leu  
                                  35                      40                      45  
 30   Lys Lys Ser Ser Met Ser Val Asp Ile Glu Asn Asn Tyr Glu Pro Gln  
                                  50                      55                      60  
 35   Tyr Ile Asn Ile Arg Gly Lys Gly Pro Leu Ile Asn Asp Leu Lys Lys  
          65                      70                      75                      80  
      Glu Ala Lys Lys Ala Asn Lys Val Phe Leu Ala Ser Asp Pro Asp Arg  
                                  85                      90                      95  
 40   Glu Gly Glu Ala Ile Ser Trp His Leu Ala His Ile Leu Asn Leu Asp  
                                  100                      105                      110  
      Glu Asn Asp Ala Asn Arg Val Val Phe Asn Glu Ile Thr Lys Asp Ala  
                                  115                      120                      125  
 45   Val Lys Asn Ala Phe Lys Glu Pro Arg Lys Ile Asp Met Asp Leu Val  
          130                      135                      140  
 50   Asp Ala Gln Gln Ala Arg Arg Ile Leu Asp Arg Leu Val Gly Tyr Ser  
      145                      150                      155                      160  
      Ile Ser Pro Ile Leu Trp Lys Lys Val Lys Lys Gly Leu Ser Ala Gly  
                                  165                      170                      175  
 55   Arg Val Gln Ser Ile Ala Leu Lys Leu Ile Ile Asp Arg Glu Asn Glu  
                                  180                      185                      190



Ile Asn Ala Phe Gln Pro Glu Glu Tyr Trp Thr Val Asp Ala Val Phe  
 195 200 205  
 5 Lys Lys Gly Thr Lys Gln Phe His Ala Ser Phe Tyr Gly Val Asp Gly  
 210 215 220  
 Lys Lys Met Lys Leu Thr Ser Asn Asn Glu Val Lys Glu Val Leu Ser  
 225 230 235 240  
 10 Arg Leu Thr Ser Lys Asp Phe Ser Val Asp Gln Val Asp Lys Lys Glu  
 245 250 255  
 Arg Lys Arg Asn Ala Pro Leu Pro Tyr Thr Thr Ser Ser Met Gln Met  
 260 265 270  
 15 Asp Ala Ala Asn Lys Ile Asn Phe Arg Thr Arg Lys Thr Met Met Val  
 275 280 285  
 20 Ala Gln Gln Leu Tyr Glu Gly Ile Asn Ile Gly Ser Gly Val Gln Gly  
 290 295 300  
 Leu Ile Thr Tyr Met Arg Thr Asp Ser Thr Arg Ile Ser Pro Val Ala  
 305 310 315 320  
 25 Gln Asn Glu Ala Ala Ser Phe Ile Thr Asp Arg Phe Gly Ser Lys Tyr  
 325 330 335  
 Ser Lys His Gly Ser Lys Val Lys Asn Ala Ser Gly Ala Gln Asp Ala  
 340 345 350  
 30 His Glu Ala Ile Arg Pro Ser Ser Val Phe Asn Thr Pro Glu Ser Ile  
 355 360 365  
 35 Ala Lys Tyr Leu Asp Lys Asp Gln Leu Lys Leu Tyr Thr Leu Ile Trp  
 370 375 380  
 Asn Arg Phe Val Ala Ser Gln Met Thr Ala Ala Val Phe Asp Thr Met  
 385 390 395 400  
 40 Ala Val Lys Leu Ser Gln Lys Gly Val Gln Phe Ala Ala Asn Gly Ser  
 405 410 415  
 Gln Val Lys Phe Asp Gly Tyr Leu Ala Ile Tyr Asn Asp Ser Asp Lys  
 420 425 430  
 45 Asn Lys Met Leu Pro Asp Met Val Val Gly Asp Val Val Lys Gln Val  
 435 440 445  
 Asn Ser Lys Pro Glu Gln His Phe Thr Gln Pro Pro Ala Arg Tyr Ser  
 450 455 460  
 Glu Ala Thr Leu Ile Lys Thr Leu Glu Glu Asn Gly Val Gly Arg Pro  
 465 470 475 480  
 55 Ser Thr Tyr Ala Pro Thr Ile Glu Thr Ile Gln Lys Arg Tyr Tyr Val  
 485 490 495

Arg Leu Ala Ala Lys Arg Phe Glu Pro Thr Glu Leu Gly Glu Ile Val  
                     500                                    505                                    510

5   sn Lys Leu Ile Val Glu Tyr Phe Pro Asp Ile Val Asn Val Thr Phe  
                     515                                    520                                    525

Thr Ala Glu Met Glu Gly Lys Leu Asp Asp Val Glu Val Gly Lys Glu  
                     530                                    535                                    540

10   Gln Trp Arg Arg Val Ile Asp Ala Phe Tyr Lys Pro Phe Ser Lys Glu  
                     545                                    550                                    555                                    560

15   Val Ala Lys Ala Glu Glu Glu Met Glu Lys Ile Gln Ile Lys Asp Glu  
                                     565                                    570                                    575

Pro Ala Gly Phe Asp Cys Glu Val Cys Gly Ser Pro Met Val Ile Lys  
                     580                                    585                                    590

20   Leu Gly Arg Phe Gly Lys Phe Tyr Ala Cys Ser Asn Phe Pro Asp Cys  
                     595                                    600                                    605

25   Arg His Thr Gln Ala Ile Val Lys Glu Ile Gly Val Glu Cys Pro Ser  
                     610                                    615                                    620

Cys His Gln Gly Gln Ile Ile Glu Arg Lys Thr Lys Arg Asn Arg Leu  
                     625                                    630                                    635                                    640

30   Phe Tyr Gly Cys Asn Arg Tyr Pro Glu Cys Glu Phe Thr Ser Trp Asp  
                                     645                                    650                                    655

Lys Pro Val Gly Arg Asp Cys Pro Lys Cys Gly Asn Phe Leu Met Glu  
                     660                                    665                                    670

35   Lys Lys Val Arg Gly Gly Gly Lys Gln Val Val Cys Ser Lys Gly Asp  
                     675                                    680                                    685

Tyr Glu Glu Glu Lys Met Ala Leu Cys Gln Leu  
                     690                                    695

40   

<210> 204  
 <211> 326  
 <212> PRT

45   <213> Streptococcus pneumoniae

<400> 204  
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                     1                                    5                                    10                                    15

50   Val Gly Ile Pro Ala Phe Ile Gln Phe Tyr Arg Lys Ala Gln Ile Thr  
                                     20                                    25                                    30

55   Gly Gln Gln Met His Glu Asp Val Lys Gln His Gln Ala Lys Ala Gly  
                     35                                    40                                    45

Thr Pro Thr Met Gly Gly Leu Val Phe Leu Ile Thr Ser Val Leu Val

50                      55                      60  
 Ala Phe Phe Phe Ala Leu Phe Ser Ser Gln Phe Ser Asn Asn Val Gly  
 65                      70                      75                      80  
 5 Met Ile Leu Phe Ile Leu Val Leu Tyr Gly Leu Val Gly Phe Leu Asp  
                                  85                      90                      95  
 10 Asp Phe Leu Lys Val Phe Arg Lys Ile Asn Glu Gly Leu Asn Pro Lys  
                                  100                      105                      110  
          Gln Lys Leu Ala Leu Gln Leu Leu Gly Gly Val Ile Phe Tyr Leu Phe  
                                  115                      120                      125  
 15 Tyr Glu Arg Gly Gly Asp Met Leu Ser Val Phe Gly Tyr Gln Val His  
                                  130                      135                      140  
          Leu Gly Ile Phe Tyr Ile Val Phe Ala Leu Phe Trp Leu Val Gly Phe  
                                  145                      150                      155                      160  
 20 Ser Asn Ala Val Asn Leu Thr Asp Gly Val Asp Gly Leu Ala Ser Ile  
                                  165                      170                      175  
 25 Ser Val Val Ile Ser Leu Ser Ala Tyr Gly Val Ile Ala Tyr Val Gln  
                                  180                      185                      190  
          Gly Gln Met Asp Ile Leu Leu Val Ile Leu Ala Met Ile Gly Gly Leu  
                                  195                      200                      205  
 30 Leu Ser Phe Phe Ile Phe Asn His Lys Pro Ala Lys Ile Phe Met Gly  
                                  210                      215                      220  
          Asp Val Gly Ser Leu Ala Leu Gly Gly Met Leu Ala Ala Ile Ser Met  
                                  225                      230                      235                      240  
 35 Ala Leu His Gln Glu Trp Thr Leu Leu Ile Ile Gly Ile Val Tyr Val  
                                  245                      250                      255  
 40 Phe Glu Thr Thr Ser Val Met Met Gln Val Ser Tyr Phe Lys Leu Thr  
                                  260                      265                      270  
          Gly Gly Lys Arg Ile Phe Arg Met Thr Pro Val His His His Phe Glu  
                                  275                      280                      285  
 45 Leu Gly Gly Leu Ser Gly Lys Gly Asn Pro Trp Ser Glu Trp Lys Val  
                                  290                      295                      300  
          Asp Phe Phe Phe Trp Gly Val Gly Leu Leu Ala Ser Leu Leu Thr Leu  
                                  305                      310                      315                      320  
 50 Ala Ile Leu Tyr Leu Met  
                                  325  
 55 <210> 205  
          <211> 693  
          <212> PRT

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 205

5 Met Ala Arg Glu Phe Ser Leu Glu Lys Thr Arg Asn Ile Gly Ile Met  
 1 5 10 15  
 Ala His Val Asp Ala Gly Lys Thr Thr Thr Thr Glu Arg Ile Leu Tyr  
 20 25 30  
 10 Tyr Thr Gly Lys Ile His Lys Ile Gly Glu Thr His Glu Gly Ala Ser  
 35 40 45  
 Gln Met Asp Trp Met Glu Gln Glu Glu Arg Gly Ile Thr Ile Thr  
 50 55 60  
 15 Ser Ala Ala Thr Thr Ala Gln Trp Asn Asn His Arg Val Asn Ile Ile  
 65 70 75 80  
 Asp Thr Pro Gly His Val Asp Phe Thr Ile Glu Val Gln Arg Ser Leu  
 85 90 95  
 Arg Val Leu Asp Gly Ala Val Thr Val Leu Asp Ser Gln Ser Gly Val  
 100 105 110  
 25 Glu Pro Gln Thr Glu Thr Val Trp Arg Gln Ala Thr Glu Tyr Gly Val  
 115 120 125  
 Pro Arg Ile Val Phe Ala Asn Lys Met Asp Lys Ile Gly Ala Asp Phe  
 130 135 140  
 30 Leu Tyr Ser Val Ser Thr Leu His Asp Arg Leu Gln Ala Asn Ala His  
 145 150 155 160  
 Pro Ile Gln Leu Pro Ile Gly Ser Glu Asp Asp Phe Arg Gly Ile Ile  
 165 170 175  
 Asp Leu Ile Lys Met Lys Ala Glu Ile Tyr Thr Asn Asp Leu Gly Thr  
 180 185 190  
 40 Asp Ile Leu Glu Glu Asp Ile Pro Ala Glu Tyr Leu Asp Gln Ala Gln  
 195 200 205  
 Glu Tyr Arg Glu Lys Leu Ile Glu Ala Val Ala Glu Thr Asp Glu Glu  
 210 215 220  
 45 Leu Met Met Lys Tyr Leu Glu Gly Glu Glu Ile Thr Asn Glu Glu Leu  
 225 230 235 240  
 Lys Ala Gly Ile Arg Lys Ala Thr Ile Asn Val Glu Phe Phe Pro Val  
 245 250 255  
 Leu Cys Gly Ser Ala Phe Lys Asn Lys Gly Val Gln Leu Met Leu Asp  
 260 265 270  
 55 Ala Val Ile Asp Tyr Leu Pro Ser Pro Leu Asp Ile Pro Ala Ile Lys  
 275 280 285

Gly Ile Asn Pro Asp Thr Asp Ala Glu Glu Ile Arg Pro Ala Ser Asp  
 290 295 300  
 5 Glu Glu Pro Phe Ala Ala Leu Ala Phe Lys Ile Met Thr Asp Pro Phe  
 305 310 315 320  
 Val Gly Arg Leu Thr Phe Phe Arg Val Tyr Ser Gly Val Leu Gln Ser  
 325 330 335  
 10 Gly Ser Tyr Val Leu Asn Thr Ser Lys Gly Lys Arg Glu Arg Ile Gly  
 340 345 350  
 Arg Ile Leu Gln Met His Ala Asn Ser Arg Gln Glu Ile Asp Thr Val  
 355 360 365  
 15 Tyr Ser Gly Asp Ile Ala Ala Val Gly Leu Lys Asp Thr Thr Thr  
 370 375 380  
 Gly Asp Ser Leu Thr Asp Glu Lys Ala Lys Ile Ile Leu Glu Ser Ile  
 20 385 390 395 400  
 Asn Val Pro Glu Pro Val Ile Gln Leu Met Val Glu Pro Lys Ser Lys  
 405 410 415  
 25 Ala Asp Gln Asp Lys Met Gly Ile Ala Leu Gln Lys Leu Ala Glu Glu  
 420 425 430  
 Asp Pro Thr Phe Arg Val Glu Thr Asn Val Glu Thr Gly Glu Thr Val  
 435 440 445  
 30 Ile Ser Gly Met Gly Glu Leu His Leu Asp Val Leu Val Asp Arg Met  
 450 455 460  
 Arg Arg Glu Phe Lys Val Glu Ala Asn Val Gly Ala Pro Gln Val Ser  
 35 465 470 475 480  
 Tyr Arg Glu Thr Phe Arg Ala Ser Thr Gln Ala Arg Gly Phe Phe Lys  
 485 490 495  
 40 Arg Gln Ser Gly Gly Lys Gly Gln Phe Gly Asp Val Trp Ile Glu Phe  
 500 505 510  
 Thr Pro Asn Glu Glu Gly Lys Gly Phe Glu Phe Glu Asn Ala Ile Val  
 515 520 525  
 45 Gly Gly Val Val Pro Arg Glu Phe Ile Pro Ala Val Glu Lys Gly Leu  
 530 535 540  
 Val Glu Ser Met Ala Asn Gly Val Leu Ala Gly Tyr Pro Met Val Asp  
 50 545 550 555 560  
 Val Lys Ala Lys Leu Tyr Asp Gly Ser Tyr His Asp Val Asp Ser Ser  
 565 570 575  
 55 Glu Thr Ala Phe Lys Ile Ala Ala Ser Leu Ser Leu Lys Glu Ala Ala  
 580 585 590

Lys Ser Ala Gln Pro Ala Ile Leu Glu Pro Met Met Leu Val Thr Ile  
 595 600 605  
 5 Thr Val Pro Glu Glu Asn Leu Gly Asp Val Met Gly His Val Thr Ala  
 610 615 620  
 Arg Arg Gly Arg Val Asp Gly Met Glu Ala His Gly Asn Ser Gln Ile  
 625 630 635 640  
 10 Val Arg Ala Tyr Val Pro Leu Ala Glu Met Phe Gly Tyr Ala Thr Val  
 645 650 655  
 Leu Arg Ser Ala Ser Gln Gly Arg Gly Thr Phe Met Met Val Phe Asp  
 660 665 670  
 15 His Tyr Glu Asp Val Pro Lys Ser Val Gln Glu Glu Ile Ile Lys Lys  
 675 680 685  
 Asn Lys Gly Glu Asp  
 20 690  
 <210> 206  
 <211> 408  
 25 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 206  
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 20 25 30  
 35 Gly Pro Lys Thr Lys Glu Leu Glu Arg Arg Leu Ser Leu Tyr Thr Gln  
 35 40 45  
 Thr Pro Lys Thr Val Cys Leu Asn Ser Ala Thr Ala Ala Leu Glu Leu  
 50 55 60  
 40 Ile Leu Arg Val Leu Glu Val Gly Pro Gly Asp Glu Val Ile Val Pro  
 65 70 75 80  
 Ala Met Thr Tyr Thr Ala Ser Cys Ser Val Ile Thr His Val Gly Ala  
 45 85 90 95  
 Thr Pro Val Met Val Asp Ile Gln Ala Asp Thr Phe Glu Met Asp Tyr  
 100 105 110  
 50 Asp Leu Leu Glu Gln Ala Ile Thr Glu Lys Thr Lys Val Ile Ile Pro  
 115 120 125  
 Val Glu Leu Ala Gly Ile Val Cys Asp Tyr Asp Arg Leu Phe Gln Val  
 130 135 140  
 55 Val Glu Lys Lys Arg Asp Phe Phe Thr Ala Ser Ser Lys Trp Gln Lys  
 145 150 155 160

Ala Phe Asn Arg Ile Val Ile Val Ser Asp Ser Ala His Ala Leu Gly  
165 170 175

5 Ser Thr Tyr Lys Gly Gln Pro Ser Gly Ser Ile Ala Asp Phe Thr Ser  
180 185 190

Phe Ser Phe His Ala Val Lys Asn Phe Thr Thr Ala Glu Gly Gly Ser  
195 200 205

10 Ala Thr Trp Lys Ala Asn Pro Val Ile Asp Asp Glu Glu Met Tyr Lys  
210 215 220

15 Glu Phe Gln Ile Leu Ser Leu His Gly Gln Thr Lys Asp Ala Leu Ala  
225 230 235 240

Lys Met Gln Leu Gly Ser Trp Glu Tyr Asp Ile Val Thr Pro Ala Tyr  
245 250 255

20 Lys Cys Asn Met Thr Asp Ile Met Ala Ser Leu Gly Leu Val Gln Leu  
260 265 270

Asp Arg Tyr Pro Ser Leu Leu Gln Arg Arg Lys Asp Ile Val Asp Arg  
275 280 285

25 Tyr Asp Ser Gly Phe Ala Gly Ser Arg Ile His Pro Leu Ala His Lys  
290 295 300

30 Thr Glu Thr Val Glu Ser Ser Arg His Leu Tyr Ile Thr Arg Val Glu  
305 310 315 320

Gly Ala Ser Leu Glu Glu Arg Ser Leu Ile Ile Gln Glu Leu Ala Lys  
325 330 335

35 Ala Gly Ile Ala Ser Asn Val His Tyr Lys Pro Leu Pro Leu Leu Thr  
340 345 350

Ala Tyr Lys Asn Leu Gly Phe Asp Met Thr Asn Tyr Pro Lys Ala Tyr  
355 360 365

40 Ala Phe Phe Glu Asn Glu Ile Thr Leu Pro Leu His Thr Lys Leu Ser  
370 375 380

45 Asp Glu Glu Val Asp Tyr Ile Ile Glu Thr Phe Lys Thr Val Ser Glu  
385 390 395 400

Lys Val Leu Thr Leu Ser Lys Lys  
405

50 <210> 207  
<211> 325  
<212> PRT  
<213> Streptococcus pneumoniae

55 <400> 207  
Met Thr Glu Pro Asp Phe Trp Asn Asp Asn Ile Ala Ala Gln Lys Thr

|    | 1   | 5   | 10  | 15  |
|----|---|-----|-----|-----|
|    | Ser Gln Glu Leu Asn Val Phe Lys Asn Thr Tyr Asn Thr Phe His Lys | 20  | 25  | 30  |
| 5  | Met Glu Glu Leu Gln Asp Glu Val Glu Ile Leu Leu Asp Phe Leu Ala | 35  | 40  | 45  |
| 10 | Glu Asp Glu Ser Val His Asp Glu Leu Val Ala Gln Leu Ala Glu Leu | 50  | 55  | 60  |
|    | Asp Lys Ile Met Thr Ser Tyr Glu Met Thr Leu Leu Leu Ser Glu Pro | 65  | 70  | 75  |
| 15 | Tyr Asp His Asn Asn Ala Ile Leu Glu Ile His Pro Gly Ser Gly Gly | 85  | 90  | 95  |
|    | Thr Glu Ala Gln Asp Trp Gly Asp Met Leu Leu Arg Met Tyr Thr Arg | 100 | 105 | 110 |
| 20 | Tyr Gly Asn Ala Lys Gly Phe Lys Val Glu Val Leu Asp Tyr Gln Ala | 115 | 120 | 125 |
|    | Gly Asp Glu Ala Gly Ile Lys Ser Val Thr Leu Ser Phe Glu Gly Pro | 130 | 135 | 140 |
| 25 | Asn Ala Tyr Gly Leu Leu Lys Ser Glu Met Gly Val His Arg Leu Val | 145 | 150 | 155 |
|    | Arg Ile Ser Pro Phe Asp Ser Ala Lys Arg Arg His Thr Ser Phe Thr | 165 | 170 | 175 |
|    | Ser Val Glu Val Met Pro Glu Leu Asp Asp Thr Ile Glu Val Glu Ile | 180 | 185 | 190 |
| 35 | Arg Glu Asp Asp Ile Lys Met Asp Thr Phe Arg Ser Gly Gly Ala Gly | 195 | 200 | 205 |
|    | Gly Gln Asn Val Asn Lys Val Ser Thr Gly Val Arg Leu Thr His Ile | 210 | 215 | 220 |
| 40 | Pro Thr Gly Ile Val Val Gln Ser Thr Val Asp Arg Thr Gln Tyr Gly | 225 | 230 | 235 |
|    | Asn Arg Asp Arg Ala Met Lys Met Leu Gln Ala Lys Leu Tyr Gln Met | 245 | 250 | 255 |
|    | Glu Gln Glu Lys Lys Ala Ala Glu Val Asp Ser Leu Lys Gly Glu Lys | 260 | 265 | 270 |
| 50 | Lys Glu Ile Thr Trp Gly Ser Gln Ile Arg Ser Tyr Val Phe Thr Pro | 275 | 280 | 285 |
|    | Tyr Thr Met Val Lys Asp His Arg Thr Ser Phe Glu Val Ala Gln Val | 290 | 295 | 300 |
| 55 | Asp Lys Val Met Asp Gly Asp Leu Asp Gly Phe Ile Asp Ala Tyr Leu |     |     |     |



159

Pro Asp Lys Lys Arg Glu Glu Leu Ala  
245

5 <210> 209  
<211> 1033  
<212> PRT  
<213> Streptococcus pneumoniae

10 <400> 209  
Met Ile Ala Gln Leu Asp Thr Lys Thr Val Tyr Ser Phe Met Glu Ser  
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15 Val Ile Ser Ile Glu Lys Tyr Val Arg Ala Ala Lys Glu Tyr Gly Tyr  
20 25 30

Thr His Leu Ala Met Met Asp Ile Asp Asn Leu Tyr Gly Ala Phe Asp  
35 40 45

20 Phe Leu Glu Ile Thr Lys Lys Tyr Gly Ile His Pro Leu Leu Gly Leu  
50 55 60

Glu Met Thr Val Phe Val Asp Asp Gln Gly Val Asn Leu Arg Phe Leu  
65 70 75 80

25 Ala Leu Ser Ser Val Gly Tyr Gln Gln Leu Met Lys Leu Ser Thr Ala  
85 90 95

30 Lys Met Gln Gly Glu Lys Thr Trp Ser Val Leu Ser Gln Tyr Leu Glu  
100 105 110

Asp Ile Ala Val Ile Val Pro Tyr Phe Asp Arg Val Glu Ser Leu Glu  
115 120 125

35 Leu Gly Cys Asp Tyr Tyr Ile Gly Val Tyr Pro Glu Thr Leu Ala Ser  
130 135 140

Glu Phe His His Pro Ile Leu Pro Leu Tyr Arg Val Asn Ala Phe Glu  
145 150 155 160

40 Ser Arg Asp Arg Glu Val Leu Gln Val Leu Thr Ala Ile Lys Glu Asn  
165 170 175

45 Leu Pro Leu Arg Glu Val Pro Leu Arg Ser Arg Gln Asp Val Phe Ile  
180 185 190

Ser Ala Ser Ser Leu Glu Lys Leu Phe Gln Glu Arg Phe Pro Gln Ala  
195 200 205

50 Leu Asp Asn Leu Glu Lys Leu Ile Ser Gly Ile Ser Tyr Asp Leu Asp  
210 215 220

Thr Ser Leu Lys Leu Pro Arg Phe Asn Pro Ala Arg Pro Ala Val Glu  
225 230 235 240

55 Glu Leu Arg Glu Arg Ala Glu Leu Gly Leu Val Gln Lys Gly Leu Thr  
245 250 255

Ser Lys Glu Tyr Gln Asp Arg Leu Asp Gln Glu Leu Ser Val Ile His  
 260 265 270  
 5 Asp Met Gly Phe Asp Asp Tyr Phe Leu Val Val Trp Asp Leu Leu Arg  
 275 280 285  
 Phe Gly Arg Ser Asn Gly Tyr Tyr Met Gly Met Gly Arg Gly Ser Ala  
 290 295 300  
 10 Val Gly Ser Leu Val Ser Tyr Ala Leu Asp Ile Thr Gly Ile Asp Pro  
 305 310 315 320  
 Val Glu Lys Asn Leu Ile Phe Glu Arg Phe Leu Asn Arg Glu Arg Tyr  
 15 325 330 335  
 Thr Met Pro Asp Ile Asp Ile Asp Ile Pro Asp Ile Tyr Arg Pro Asp  
 340 345 350  
 20 Phe Ile Arg Tyr Val Gly Asn Lys Tyr Gly Ser Lys His Ala Ala Gln  
 355 360 365  
 Ile Val Thr Phe Ser Thr Phe Gly Ala Lys Gln Ala Leu Arg Asp Val  
 370 375 380  
 25 Leu Lys Arg Phe Gly Val Pro Glu Tyr Glu Leu Ser Ala Ile Thr Lys  
 385 390 395 400  
 Lys Ile Ser Phe Arg Asp Asn Leu Lys Ser Ala Tyr Glu Gly Asn Leu  
 30 405 410 415  
 Gln Phe Arg Gln Gln Ile Asn Ser Lys Leu Glu Tyr Gln Lys Ala Phe  
 420 425 430  
 35 Glu Ile Ala Cys Lys Ile Glu Gly Tyr Pro Arg Gln Thr Ser Val His  
 435 440 445  
 Ala Ala Gly Val Val Ile Ser Asp Gln Asp Leu Thr Asn Tyr Ile Pro  
 450 455 460  
 40 Leu Lys Tyr Gly Asp Glu Ile Pro Leu Thr Gln Tyr Asp Ala His Gly  
 465 470 475 480  
 Val Glu Ala Ser Gly Leu Leu Lys Met Asp Phe Leu Gly Leu Arg Asn  
 45 485 490 495  
 Leu Thr Phe Val Gln Lys Met Gln Glu Leu Leu Ala Glu Ile Glu Gly  
 500 505 510  
 50 Ile His Leu Lys Ile Glu Glu Ile Asp Leu Glu Asp Lys Glu Thr Leu  
 515 520 525  
 Asp Leu Phe Ala Ser Gly Asn Thr Lys Gly Ile Phe Gln Phe Glu Gln  
 530 535 540  
 55 Pro Gly Ala Ile Arg Leu Leu Lys Arg Val Gln Pro Val Cys Phe Glu  
 545 550 555 560

Asp Val Val Ala Thr Thr Ser Leu Asn Arg Pro Gly Ala Ser Asp Tyr  
 565 570 575  
 5 Ile Asn Asn Phe Val Ala Arg Lys His Gly Gln Glu Glu Val Thr Val  
 580 585 590  
 Leu Asp Pro Val Leu Glu Asp Ile Leu Ala Pro Thr Tyr Gly Ile Met  
 595 600 605  
 10 Leu Tyr Gln Glu Gln Val Met Gln Val Ala Gln Arg Phe Ala Gly Phe  
 610 615 620  
 Ser Leu Gly Lys Ala Asp Ile Leu Arg Arg Ala Met Gly Lys Lys Asp  
 15 625 630 635 640  
 Ala Ser Ala Met His Glu Met Arg Ala Ser Phe Ile Gln Gly Ser Leu  
 645 650 655  
 20 Glu Ala Gly His Thr Val Glu Lys Ala Glu Gln Val Phe Asp Val Met  
 660 665 670  
 Glu Lys Phe Ala Gly Tyr Gly Phe Asn Arg Ser His Ala Tyr Ala Tyr  
 675 680 685  
 25 Ser Ala Leu Ala Phe Gln Leu Ala Tyr Phe Lys Thr His Tyr Pro Ala  
 690 695 700  
 Ile Phe Tyr Gln Ile Met Leu Asn Ser Ala Asn Ser Asp Tyr Leu Ile  
 30 705 710 715 720  
 Asp Ala Leu Glu Ala Gly Phe Glu Val Ala Pro Leu Ser Ile Asn Thr  
 725 730 735  
 35 Ile Pro Tyr His Asp Lys Ile Ala Asn Lys Ala Ile Tyr Leu Gly Leu  
 740 745 750  
 Lys Ser Ile Lys Gly Val Ser Asn Asp Leu Ala Leu Trp Ile Ile Glu  
 755 760 765  
 40 His Arg Pro Tyr Ser Asn Ile Glu Asp Phe Ile Ala Lys Leu Pro Glu  
 770 775 780  
 Asn Tyr Leu Lys Leu Pro Leu Leu Glu Pro Leu Val Lys Val Gly Leu  
 45 785 790 795 800  
 Phe Asp Ser Phe Glu Lys Asn Arg Gln Lys Val Phe Asn Asn Leu Ala  
 805 810 815  
 50 Asn Leu Phe Glu Phe Val Lys Glu Leu Gly Ser Leu Phe Gly Asp Ala  
 820 825 830  
 Ile Tyr Ser Trp Gln Glu Ser Glu Asp Trp Thr Glu Gln Glu Lys Phe  
 835 840 845  
 55 Tyr Met Glu Gln Glu Leu Leu Gly Ile Gly Val Ser Lys His Pro Leu  
 850 855 860

Gln Ala Ile Ala Ser Lys Ala Ile Tyr Pro Ile Thr Pro Ile Gly Asn  
 865 870 875 880  
 5 Leu Ser Glu Asn Ser Tyr Ala Ile Ile Leu Val Glu Val Gln Lys Ile  
 885 890 895  
 Lys Val Ile Arg Thr Lys Lys Gly Glu Asn Met Ala Phe Leu Gln Ala  
 900 905 910  
 10 Asp Asp Ser Lys Lys Lys Leu Asp Val Thr Leu Phe Ser Asp Leu Tyr  
 915 920 925  
 15 Arg Gln Val Gly Gln Glu Ile Lys Glu Gly Ala Phe Tyr Tyr Val Lys  
 930 935 940  
 Gly Lys Ile Gln Ser Arg Asp Gly Arg Leu Gln Met Ile Ala Gln Glu  
 945 950 955 960  
 20 Ile Arg Glu Ala Val Ala Glu Arg Phe Trp Ile Gln Val Lys Asn His  
 965 970 975  
 Glu Ser Asp Gln Glu Ile Ser Arg Ile Leu Glu Gln Phe Lys Gly Pro  
 980 985 990  
 25 Ile Pro Val Ile Ile Arg Tyr Glu Glu Glu Gln Lys Thr Ile Val Ser  
 995 1000 1005  
 30 Pro His His Phe Val Ala Lys Ser Asn Glu Leu Glu Glu Lys Leu Asn  
 1010 1015 1020  
 Glu Ile Val Met Lys Thr Ile Tyr Arg  
 1025 1030  
 35  
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 <211> 306  
 <212> PRT  
 <213> Streptococcus pneumoniae  
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 <400> 210  
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 45 Gln Ser Leu His Arg Lys Thr Thr Pro Pro Leu Thr Glu Glu Glu Leu  
 20 25 30  
 Glu Ser Ile Lys Ser Phe Asn Asp Gln Ile Ser Leu Gln Asp Val Thr  
 35 40 45  
 50 Asp Ile Tyr Leu Pro Leu Ala His Leu Ile Gln Ile Tyr Lys Arg Thr  
 50 55 60  
 55 Lys Glu Asp Leu Ala Phe Ser Lys Gly Ile Phe Leu Gln Arg Glu Ser  
 65 70 75 80  
 Lys Ser Gln Pro Phe Ile Ile Gly Val Ser Gly Ser Val Ala Val Gly

|    | 85  | 90  | 95  |
|----|---|-----|-----|
|    | Lys Ser Thr Thr Ser Arg Leu Leu Gln Ile Leu Leu Ser Arg Thr Phe |     |     |
|    | 100   | 105 | 110 |
| 5  | Thr Asp Ala Thr Val Glu Leu Val Thr Thr Asp Gly Phe Leu Tyr Pro |     |     |
|    | 115   | 120 | 125 |
| 10 | Asn Gln Thr Leu Ile Glu Gln Gly Ile Leu Asn Arg Lys Gly Phe Pro |     |     |
|    | 130   | 135 | 140 |
|    | Glu Ser Tyr Asp Met Glu Ala Leu Leu Asn Phe Leu Asp Arg Ile Lys |     |     |
|    | 145   | 150 | 155 |
| 15 | Asn Gly Gln Asp Val Asp Ile Pro Val Tyr Ser His Glu Val Tyr Asp |     |     |
|    | 165   | 170 | 175 |
|    | Ile Val Pro Lys Lys Lys Gln Ser Val Lys Ala Ala Asp Phe Val Ile |     |     |
|    | 180   | 185 | 190 |
| 20 | Val Glu Gly Ile Asn Val Phe Gln Asn Pro Gln Asn Asp Arg Leu Tyr |     |     |
|    | 195   | 200 | 205 |
|    | Ile Thr Asp Phe Phe Asp Phe Ser Ile Tyr Val Asp Ala Gly Val Asp |     |     |
| 25 | 210   | 215 | 220 |
|    | Asp Ile Glu Ser Trp Tyr Leu Asp Arg Phe Leu Lys Met Leu Ser Leu |     |     |
|    | 225   | 230 | 235 |
| 30 | Ala Gln Asn Asp Pro Asp Ser Tyr Tyr Tyr Arg Phe Thr Gln Met Pro |     |     |
|    | 245   | 250 | 255 |
|    | Ile Gly Glu Val Glu Ser Phe Ala His Gln Val Trp Thr Ser Ile Asn |     |     |
|    | 260   | 265 | 270 |
| 35 | Leu Thr Asn Leu Gln Asn Tyr Ile Glu Pro Thr Arg Asn Arg Ala Glu |     |     |
|    | 275   | 280 | 285 |
|    | Val Ile Leu His Lys Ser Lys Asn His Glu Ile Asp Glu Ile Tyr Leu |     |     |
| 40 | 290   | 295 | 300 |
|    | Lys Lys   |     |     |
|    | 305   |     |     |
| 45 |   |     |     |
|    | <210> 211   |     |     |
|    | <211> 246   |     |     |
|    | <212> PRT   |     |     |
|    | <213> Streptococcus pneumoniae                                  |     |     |
| 50 |   |     |     |
|    | <400> 211   |     |     |
|    | Met Glu Ile Ser Leu Leu Thr Asp Val Gly Gln Lys Arg Thr Asn Asn |     |     |
|    | 1   | 5   | 10  |
| 55 | Gln Asp Tyr Val Asn His Tyr Val Asn Arg Ala Gly Arg Thr Met Ile |     |     |
|    | 20  | 25  | 30  |

Ile Leu Ala Asp Gly Met Gly Gly His Arg Ala Gly Asn Ile Ala Ser  
                   35                                  40                                  45  
 5   Glu Met Ala Val Thr Asp Leu Gly Val Ala Trp Val Asp Thr Gln Ile  
           50                                  55                                  60  
 Asp Thr Val Asn Glu Val Arg Glu Trp Phe Ala His Tyr Leu Glu Ile  
           65                                  70                                  75                                  80  
 10   Glu Asn Gln Lys Ile His Gln Leu Gly Gln Asp Glu Ala Tyr Arg Gly  
                                   85                                  90                                  95  
 Met Gly Thr Thr Leu Glu Val Leu Ala Ile Ile Asp Asn Gln Ala Ile  
                                   100                                  105                                  110  
 15   Tyr Ala His Ile Gly Asp Ser Arg Ile Gly Leu Ile Arg Gly Glu Glu  
                                   115                                  120                                  125  
 Tyr His Gln Leu Thr Ser Asp His Ser Leu Val Asn Glu Leu Leu Lys  
           130                                  135                                  140  
 Ala Gly Gln Leu Thr Pro Glu Glu Ala Glu Ala His Pro Gln Lys Asn  
           145                                  150                                  155                                  160  
 25   Ile Ile Thr Gln Ser Ile Gly Gln Lys Asp Glu Ile Gln Pro Asp Phe  
                                   165                                  170                                  175  
 Gly Thr Val Ile Leu Glu Ser Gly Asp Tyr Leu Leu Leu Asn Ser Asp  
                                   180                                  185                                  190  
 30   Gly Leu Thr Asn Met Ile Ser Gly Ser Glu Ile Arg Asp Ile Val Thr  
                                   195                                  200                                  205  
 Ser Asp Ile Pro Leu Ala Asp Lys Thr Glu Thr Leu Val Arg Phe Ala  
           210                                  215                                  220  
 Asn Asn Ala Gly Gly Leu Asp Asn Ile Thr Val Ala Leu Val Ser Met  
           225                                  230                                  235                                  240  
 40   Asn Glu Glu Asp Glu Glu  
                                   245  
 45   <210> 212  
       <211> 276  
       <212> PRT  
       <213> Streptococcus pneumoniae  
 50   <400> 212  
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 Asn Arg Lys Pro Gln Ser Gln Arg Val Leu Tyr Glu Leu Arg Asp Arg  
                                   20                                  25                                  30  
 55   Leu Lys Arg Asn Gln Phe Ile Leu Asn Asp Thr Asn Pro Asp Ile Val  
           35                                  40                                  45

Ile Ser Ile Gly Gly Asp Gly Met Leu Leu Ser Ala Phe His Lys Tyr  
 50 55 60  
 5 Glu Asn Gln Leu Asp Lys Val Arg Phe Ile Gly Leu His Thr Gly His  
 65 70 75 80  
 Leu Gly Phe Tyr Thr Asp Tyr Arg Asp Phe Glu Leu Asp Lys Leu Val  
 85 90 95  
 10 Thr Asn Leu Gln Leu Asp Thr Gly Ala Arg Val Ser Tyr Pro Val Leu  
 100 105 110  
 15 Asn Val Lys Val Phe Leu Glu Asn Gly Glu Val Lys Ile Phe Arg Ala  
 115 120 125  
 Leu Asn Glu Ala Ser Ile Arg Arg Ser Asp Arg Thr Met Val Ala Asp  
 130 135 140  
 20 Ile Val Ile Asn Gly Val Pro Phe Glu Arg Phe Arg Gly Asp Gly Leu  
 145 150 155 160  
 Thr Val Ser Thr Pro Thr Gly Ser Thr Ala Tyr Asn Lys Ser Leu Gly  
 165 170 175  
 25 Gly Ala Val Leu His Pro Thr Ile Glu Ala Leu Gln Leu Thr Glu Ile  
 180 185 190  
 30 Ala Ser Leu Asn Asn Arg Val Tyr Arg Thr Leu Gly Ser Ser Ile Ile  
 195 200 205  
 Val Pro Lys Lys Asp Lys Ile Glu Leu Ile Pro Thr Arg Asn Asp Tyr  
 210 215 220  
 35 His Thr Ile Ser Val Asp Asn Ser Val Tyr Ser Phe Arg Asn Ile Glu  
 225 230 235 240  
 Arg Ile Glu Tyr Gln Ile Asp His His Lys Ile His Phe Val Ala Thr  
 245 250 255  
 40 Pro Ser His Thr Ser Phe Trp Asn Arg Val Lys Asp Ala Phe Ile Gly  
 260 265 270  
 45 Glu Val Asp Glu  
 275  
 <210> 213  
 <211> 540  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 213  
 55 Met Ser Lys Glu Ile Lys Phe Ser Ser Asp Ala Arg Ser Ala Met Val  
 1 5 10 15  
 Arg Gly Val Asp Ile Leu Ala Asp Thr Val Lys Val Thr Leu Gly Pro



|    | 20  | 25  | 30  |
|----|---|-----|-----|
|    | Lys Gly Arg Asn Val Val Leu Glu Lys Ser Phe Gly Ser Pro Leu Ile |     |     |
|    | 35  | 40  | 45  |
| 5  | Thr Asn Asp Gly Val Thr Ile Ala Lys Glu Ile Glu Leu Glu Asp His |     |     |
|    | 50  | 55  | 60  |
| 10 | Phe Glu Asn Met Gly Ala Lys Leu Val Ser Glu Val Ala Ser Lys Thr |     |     |
|    | 65  | 70  | 75  |
|    | Asn Asp Ile Ala Gly Asp Gly Thr Thr Thr Ala Thr Val Leu Thr Gln |     |     |
|    | 85  | 90  | 95  |
| 15 | Ala Ile Val Arg Glu Gly Ile Lys Asn Val Thr Ala Gly Ala Asn Pro |     |     |
|    | 100   | 105 | 110 |
|    | Ile Gly Ile Arg Arg Gly Ile Glu Thr Ala Val Ala Ala Val Glu     |     |     |
|    | 115   | 120 | 125 |
| 20 | Ala Leu Lys Asn Asn Ala Ile Pro Val Ala Asn Lys Glu Ala Ile Ala |     |     |
|    | 130   | 135 | 140 |
|    | Gln Val Ala Ala Val Ser Ser Arg Ser Glu Lys Val Gly Glu Tyr Ile |     |     |
| 25 | 145   | 150 | 155 |
|    | Ser Glu Ala Met Glu Lys Val Gly Lys Asp Gly Val Ile Thr Ile Glu |     |     |
|    | 165   | 170 | 175 |
| 30 | Glu Ser Arg Gly Met Glu Thr Glu Leu Glu Val Val Glu Gly Met Gln |     |     |
|    | 180   | 185 | 190 |
|    | Phe Asp Arg Gly Tyr Leu Ser Gln Tyr Met Val Thr Asp Ser Glu Lys |     |     |
|    | 195   | 200 | 205 |
| 35 | Met Val Ala Asp Leu Glu Asn Pro Tyr Ile Leu Ile Thr Asp Lys Lys |     |     |
|    | 210   | 215 | 220 |
|    | Ile Ser Asn Ile Gln Glu Ile Leu Pro Leu Leu Glu Ser Ile Leu Gln |     |     |
| 40 | 225   | 230 | 235 |
|    | Ser Asn Arg Pro Leu Leu Ile Ile Ala Asp Asp Val Asp Gly Glu Ala |     |     |
|    | 245   | 250 | 255 |
| 45 | Leu Pro Thr Leu Val Leu Asn Lys Ile Arg Gly Thr Phe Asn Val Val |     |     |
|    | 260   | 265 | 270 |
|    | Ala Val Lys Ala Pro Gly Phe Gly Asp Arg Arg Lys Ala Met Leu Glu |     |     |
|    | 275   | 280 | 285 |
| 50 | Asp Ile Ala Ile Leu Thr Gly Gly Thr Val Ile Thr Glu Asp Leu Gly |     |     |
|    | 290   | 295 | 300 |
|    | Leu Glu Leu Lys Asp Ala Thr Ile Glu Ala Leu Gly Gln Ala Ala Arg |     |     |
| 55 | 305   | 310 | 315 |
|    | Val Thr Val Asp Lys Asp Ser Thr Val Ile Val Glu Gly Ala Gly Asn |     |     |

|    |   |  |     |  |     |
|----|---|--|-----|--|-----|
|    | 325   |  | 330 |  | 335 |
|    | Pro Glu Ala Ile Ser His Arg Val Ala Val Ile Lys Ser Gln Ile Glu |  |     |  |     |
|    | 340   |  | 345 |  | 350 |
| 5  | Thr Thr Thr Ser Glu Phe Asp Arg Glu Lys Leu Gln Glu Arg Leu Ala |  |     |  |     |
|    | 355   |  | 360 |  | 365 |
| 10 | Lys Leu Ser Gly Gly Val Ala Val Ile Lys Val Gly Ala Ala Thr Glu |  |     |  |     |
|    | 370   |  | 375 |  | 380 |
|    | Thr Glu Leu Lys Glu Met Lys Leu Arg Ile Glu Asp Ala Leu Asn Ala |  |     |  |     |
|    | 385   |  | 390 |  | 395 |
| 15 | Thr Arg Ala Ala Val Glu Glu Gly Ile Val Ala Gly Gly Gly Thr Ala |  |     |  |     |
|    | 405   |  | 410 |  | 415 |
|    | Leu Ala Asn Val Ile Pro Ala Val Ala Thr Leu Glu Leu Thr Gly Asp |  |     |  |     |
| 20 | 420   |  | 425 |  | 430 |
|    | Glu Ala Thr Gly Arg Asn Ile Val Leu Arg Ala Leu Glu Glu Pro Val |  |     |  |     |
|    | 435   |  | 440 |  | 445 |
| 25 | Arg Gln Ile Ala His Asn Ala Gly Phe Glu Gly Ser Ile Val Ile Asp |  |     |  |     |
|    | 450   |  | 455 |  | 460 |
|    | Arg Leu Lys Asn Ala Glu Leu Gly Ile Gly Phe Asn Ala Ala Thr Gly |  |     |  |     |
|    | 465   |  | 470 |  | 475 |
| 30 | Glu Trp Val Asn Met Ile Asp Gln Gly Ile Ile Asp Pro Val Lys Val |  |     |  |     |
|    | 485   |  | 490 |  | 495 |
|    | Ser Arg Ser Ala Leu Gln Asn Ala Ala Ser Val Ala Ser Leu Ile Leu |  |     |  |     |
| 35 | 500   |  | 505 |  | 510 |
|    | Thr Thr Glu Ala Val Val Ala Asn Lys Pro Glu Pro Val Ala Pro Ala |  |     |  |     |
|    | 515   |  | 520 |  | 525 |
| 40 | Pro Ala Met Asp Pro Ser Met Met Gly Gly Met Met                 |  |     |  |     |
|    | 530   |  | 535 |  | 540 |
| 45 | <210> 214   |  |     |  |     |
|    | <211> 481   |  |     |  |     |
|    | <212> PRT   |  |     |  |     |
|    | <213> Streptococcus pneumoniae                                  |  |     |  |     |
| 50 | <400> 214   |  |     |  |     |
|    | Met Ile Lys Ile Glu Thr Val Leu Asp Ile Leu Lys Lys Asp Gly Leu |  |     |  |     |
|    | 1   |  | 5   |  | 10  |
|    | Phe Arg Glu Ile Ile Asp Gln Gly His Tyr His Tyr Asn Tyr Ser Lys |  |     |  |     |
|    | 20  |  | 25  |  | 30  |
| 55 | Val Ile Phe Asp Ser Ile Ser Tyr Asp Ser Arg Lys Val Thr Glu Asp |  |     |  |     |
|    | 35  |  | 40  |  | 45  |

Thr Leu Phe Phe Ala Lys Gly Ala Ala Phe Lys Lys Glu Tyr Leu Leu  
 50 55 60  
 5 Ser Ala Ile Thr Gln Gly Leu Ala Trp Tyr Val Ala Glu Lys Asp Tyr  
 65 70 75 80  
 Glu Val Gly Ile Pro Val Ile Ile Val Asn Asp Ile Lys Lys Ala Met  
 85 90 95  
 10 Ser Leu Ile Ala Met Glu Phe Tyr Gly Asn Pro Gln Glu Lys Leu Lys  
 100 105 110  
 Leu Leu Ala Phe Thr Gly Thr Lys Gly Lys Thr Thr Ala Ala Tyr Phe  
 115 120 125  
 15 Ala Tyr Asn Ile Leu Ser Gln Gly His Arg Pro Ala Met Leu Ser Thr  
 130 135 140  
 Met Asn Thr Thr Leu Asp Gly Glu Thr Phe Phe Lys Ser Ala Leu Thr  
 145 150 155 160  
 Thr Pro Glu Ser Ile Asp Leu Phe Asp Met Met Asn Gln Ala Val Gln  
 165 170 175  
 25 Asn Asp Arg Thr His Leu Ile Met Glu Val Ser Ser Gln Ala Tyr Leu  
 180 185 190  
 Val Lys Arg Val Tyr Gly Leu Thr Phe Asp Val Gly Val Phe Leu Asn  
 195 200 205  
 30 Ile Ser Pro Asp His Ile Gly Pro Ile Glu His Pro Ser Phe Glu Asp  
 210 215 220  
 Tyr Phe Tyr His Lys Arg Leu Leu Met Glu Lys Ser Arg Ala Val Ile  
 225 230 235 240  
 Ile Asn Ser Asp Met Asp His Phe Ser Val Leu Lys Glu Gln Val Glu  
 245 250 255  
 40 Asp Gln Asp His Asp Phe Tyr Gly Ser Gln Phe Asp Asn Gln Ile Glu  
 260 265 270  
 Asn Ser Lys Ala Phe Ser Phe Ser Ala Thr Gly Lys Leu Ala Gly Asp  
 275 280 285  
 45 Tyr Asp Ile Gln Leu Ile Gly Asn Phe Asn Gln Glu Asn Ala Val Ala  
 290 295 300  
 Ala Gly Leu Ala Cys Leu Arg Leu Gly Ala Ser Leu Glu Asp Ile Lys  
 305 310 315 320  
 Lys Gly Ile Ala Ala Thr Arg Val Pro Gly Arg Met Glu Val Leu Thr  
 325 330 335  
 55 Gln Lys Asn Gly Ala Lys Val Phe Ile Asp Tyr Ala His Asn Gly Asp  
 340 345 350

Ser Leu Lys Lys Leu Ile Asn Val Val Glu Thr His Gln Thr Gly Lys  
 355 360 365  
 5 Ile Ala Leu Val Leu Gly Ser Thr Gly Asn Lys Gly Glu Ser Arg Arg  
 370 375 380  
 Lys Asp Phe Gly Leu Leu Leu Asn Gln His Pro Glu Ile Gln Val Phe  
 385 390 395 400  
 10 Leu Thr Ala Asp Asp Pro Asn Tyr Glu Asp Pro Met Ala Ile Ala Asp  
 405 410 415  
 Glu Ile Ser Ser Tyr Ile Asn His Pro Val Glu Lys Ile Ala Asp Arg  
 420 425 430  
 15 Gln Glu Ala Ile Lys Ala Ala Met Ala Ile Thr Asn His Glu Leu Asp  
 435 440 445  
 Ala Val Ile Ile Ala Gly Lys Gly Ala Asp Cys Tyr Gln Ile Ile Gln  
 450 455 460  
 20 Gly Lys Lys Glu Ser Tyr Pro Gly Asp Thr Ala Val Ala Glu Asn Tyr  
 465 470 475 480  
 25 Leu  
 30 <210> 215  
 <211> 659  
 <212> PRT  
 <213> Streptococcus pneumoniae  
 35 <400> 215  
 Met Ile Gln Ile Gly Lys Ile Phe Ala Gly Arg Tyr Arg Ile Val Lys  
 1 5 10 15  
 Gln Ile Gly Arg Gly Gly Met Ala Asp Val Tyr Leu Ala Lys Asp Leu  
 20 25 30  
 40 Ile Leu Asp Gly Glu Glu Val Ala Val Lys Val Leu Arg Thr Asn Tyr  
 35 40 45  
 Gln Thr Asp Pro Ile Ala Val Ala Arg Phe Gln Arg Glu Ala Arg Ala  
 45 50 55 60  
 Met Ala Asp Leu Asp His Pro His Ile Val Arg Ile Thr Asp Ile Gly  
 65 70 75 80  
 50 Glu Glu Asp Gly Gln Gln Tyr Leu Ala Met Glu Tyr Val Ala Gly Leu  
 85 90 95  
 Asp Leu Lys Arg Tyr Ile Lys Glu His Tyr Pro Leu Ser Asn Glu Glu  
 100 105 110  
 55 Ala Val Arg Ile Met Gly Gln Ile Leu Leu Ala Met Arg Leu Ala His  
 115 120 125

Thr Arg Gly Ile Val His Arg Asp Leu Lys Pro Gln Asn Ile Leu Leu  
 130 135 140

5 Thr Pro Asp Gly Thr Ala Lys Val Thr Asp Phe Gly Ile Ala Val Ala  
 145 150 155 160

Phe Ala Glu Thr Ser Leu Thr Gln Thr Asn Ser Met Leu Gly Ser Val  
 165 170 175

10 His Tyr Leu Ser Pro Glu Gln Ala Arg Gly Ser Lys Ala Thr Val Gln  
 180 185 190

15 Ser Asp Ile Tyr Ala Met Gly Ile Ile Phe Tyr Glu Met Leu Thr Gly  
 195 200 205

His Ile Pro Tyr Asp Gly Asp Ser Ala Val Thr Ile Ala Leu Gln His  
 210 215 220

20 Phe Gln Lys Pro Leu Pro Ser Val Ile Ala Glu Asn Pro Ser Val Pro  
 225 230 235 240

Gln Ala Leu Glu Asn Val Ile Ile Lys Ala Thr Ala Lys Lys Leu Thr  
 245 250 255

25 Asn Arg Tyr Arg Ser Val Ser Glu Met Tyr Val Asp Leu Ser Ser Ser  
 260 265 270

30 Leu Ser Tyr Asn Arg Arg Asn Glu Ser Lys Leu Ile Phe Asp Glu Thr  
 275 280 285

Ser Lys Ala Asp Thr Lys Thr Leu Pro Lys Val Ser Gln Ser Thr Leu  
 290 295 300

35 Thr Ser Ile Pro Lys Val Gln Ala Gln Thr Glu His Lys Ser Ile Lys  
 305 310 315 320

Asn Pro Ser Gln Ala Val Thr Glu Glu Thr Tyr Gln Pro Gln Ala Pro  
 325 330 335

40 Lys Lys His Arg Phe Lys Met Arg Tyr Leu Ile Leu Leu Ala Ser Leu  
 340 345 350

Val Leu Val Ala Ala Ser Leu Ile Trp Ile Leu Ser Arg Thr Pro Ala  
 355 360 365

Thr Ile Ala Ile Pro Asp Val Ala Gly Gln Thr Val Ala Glu Ala Lys  
 370 375 380

50 Ala Thr Leu Lys Lys Ala Asn Phe Glu Ile Gly Glu Glu Lys Thr Glu  
 385 390 395 400

Ala Ser Glu Lys Val Glu Glu Gly Arg Ile Ile Arg Thr Asp Pro Gly  
 405 410 415

55 Ala Gly Thr Gly Arg Lys Glu Gly Thr Lys Ile Asn Leu Val Val Ser  
 420 425 430

Ser Gly Lys Gln Ser Phe Gln Ile Ser Asn Tyr Val Gly Arg Lys Ser  
 435 440 445  
 5 Ser Asp Val Ile Ala Glu Leu Lys Glu Lys Lys Val Pro Asp Asn Leu  
 450 455 460  
 Ile Lys Ile Glu Glu Glu Glu Ser Asn Glu Ser Glu Ala Gly Thr Val  
 465 470 475 480  
 10 Leu Lys Gln Ser Leu Pro Glu Gly Thr Thr Tyr Asp Leu Ser Lys Ala  
 485 490 495  
 Thr Gln Ile Val Leu Thr Val Ala Lys Lys Ala Thr Thr Ile Gln Leu  
 15 500 505 510  
 Gly Asn Tyr Ile Gly Arg Asn Ser Thr Glu Val Ile Ser Glu Leu Lys  
 515 520 525  
 20 Gln Lys Lys Val Pro Glu Asn Leu Ile Lys Ile Glu Glu Glu Glu Ser  
 530 535 540  
 Ser Glu Ser Glu Pro Gly Thr Ile Met Lys Gln Ser Pro Gly Ala Gly  
 545 550 555 560  
 25 Thr Thr Tyr Asp Val Ser Lys Pro Thr Gln Ile Val Leu Thr Val Ala  
 565 570 575  
 Lys Lys Val Thr Ser Val Ala Met Pro Ser Tyr Ile Gly Ser Ser Leu  
 30 580 585 590  
 Glu Phe Thr Lys Asn Asn Leu Ile Gln Ile Val Gly Ile Lys Glu Ala  
 595 600 605  
 35 Asn Ile Glu Val Val Glu Val Thr Thr Ala Pro Ala Gly Ser Ala Glu  
 610 615 620  
 Gly Met Val Val Glu Gln Ser Pro Arg Ala Gly Glu Lys Val Asp Leu  
 625 630 635 640  
 40 Asn Lys Thr Arg Val Lys Ile Ser Ile Tyr Lys Pro Lys Thr Thr Ser  
 645 650 655  
 Ala Thr Pro  
 45  
 <210> 216  
 <211> 391  
 50 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 216  
 Met Lys His Phe Asp Thr Ile Val Ile Gly Gly Gly Pro Ala Gly Met  
 55 1 5 10 15  
 Met Ala Thr Ile Ser Ser Asn Phe Tyr Gly Gln Lys Thr Leu Leu Ile

|    | 20  | 25                              | 30          |
|----|---|---------------------------------|-------------|
|    | Glu Lys Asn Arg Lys Leu Gly                                     | Lys Lys Leu Ala Gly Thr         | Gly Gly Gly |
|    | 35  | 40                              | 45          |
| 5  | Arg Cys Asn Val Thr Asn Asn Gly                                 | Ser Leu Asp Asn Leu Leu Ala Gly |             |
|    | 50  | 55                              | 60          |
| 10 | Ile Pro Gly Asn Gly Arg Phe Leu Tyr Ser Val Phe Ser Gln Phe Asp |                                 |             |
|    | 65  | 70                              | 75          |
|    | Asn His Asp Ile Ile Asn Phe Phe Thr Glu Asn Gly Val Lys Leu Lys |                                 |             |
|    | 85  | 90                              | 95          |
| 15 | Val Glu Asp His Gly Arg Val Phe Pro Ala Ser Asp Lys Ser Arg Thr |                                 |             |
|    | 100   | 105                             | 110         |
|    | Ile Ile Glu Ala Leu Glu Lys Lys Ile Thr Glu Leu Gly Gly Gln Val |                                 |             |
|    | 115   | 120                             | 125         |
| 20 | Ala Thr Gln Ile Glu Ile Val Ser Val Lys Lys Val Asp Asp Gln Phe |                                 |             |
|    | 130   | 135                             | 140         |
| 25 | Val Leu Lys Ser Ala Asp Gln Thr Phe Thr Cys Glu Lys Leu Ile Val |                                 |             |
|    | 145   | 150                             | 155         |
|    | Thr Thr Gly Gly Lys Ser Tyr Pro Ser Thr Gly Ser Thr Gly Phe Gly |                                 |             |
|    | 165   | 170                             | 175         |
| 30 | His Glu Ile Ala Arg His Phe Lys His Thr Ile Thr Asp Leu Glu Ala |                                 |             |
|    | 180   | 185                             | 190         |
|    | Ala Glu Ser Pro Leu Leu Thr Asp Phe Pro His Lys Ala Leu Gln Gly |                                 |             |
|    | 195   | 200                             | 205         |
| 35 | Ile Ser Leu Asp Asp Val Thr Leu Ser Tyr Gly Lys His Val Ile Thr |                                 |             |
|    | 210   | 215                             | 220         |
| 40 | His Asp Leu Leu Phe Thr His Phe Gly Leu Ser Gly Pro Ala Ala Leu |                                 |             |
|    | 225   | 230                             | 235         |
|    | Arg Met Ser Ser Phe Val Lys Gly Gly Glu Val Leu Ser Leu Asp Val |                                 |             |
|    | 245   | 250                             | 255         |
| 45 | Leu Pro Gln Leu Ser Glu Lys Asp Leu Val Thr Phe Leu Glu Glu Asn |                                 |             |
|    | 260   | 265                             | 270         |
|    | Arg Glu Lys Ser Leu Lys Asn Ala Leu Lys Thr Leu Leu Pro Glu Arg |                                 |             |
|    | 275   | 280                             | 285         |
| 50 | Leu Ala Glu Phe Phe Val Gln Gly Tyr Pro Glu Lys Val Lys Gln Leu |                                 |             |
|    | 290   | 295                             | 300         |
| 55 | Thr Glu Lys Glu Arg Glu Gln Leu Val Gln Ser Ile Lys Glu Leu Lys |                                 |             |
|    | 305   | 310                             | 315         |
|    | Ile Pro Val Thr Gly Lys Met Ser Leu Ala Lys Ser Phe Val Thr Lys |                                 |             |

174



Ala Tyr Val Glu His Val Leu Pro Glu Lys Met Arg Tyr Asn Leu Ala  
 195 200 205

5 Tyr Leu Arg Glu Phe Ser Phe Phe Gly Asp Ile Lys Ile Met Phe Gln  
 210 215 220

Thr Val Phe Glu Val Leu Lys  
 225 230

10 <210> 218  
 <211> 140  
 <212> PRT  
 <213> Streptococcus pneumoniae

15 <400> 218  
 Met Thr Ser Pro Leu Leu Glu Ser Arg Arg Gln Leu Arg Lys Cys Ala  
 1 5 10 15

20 Phe Gln Ala Leu Met Ser Leu Glu Phe Gly Thr Asp Val Glu Thr Ala  
 20 25 30

Cys Arg Phe Ala Tyr Thr His Asp Arg Glu Tyr Thr Asp Val Gln Leu  
 35 40 45

25 Pro Ala Phe Leu Ile Asp Leu Val Ser Gly Val Gln Ala Lys Lys Glu  
 50 55 60

30 Glu Leu Asp Lys Gln Ile Thr Gln His Leu Lys Ala Gly Trp Thr Ile  
 65 70 75 80

Glu Arg Leu Thr Leu Val Glu Arg Asn Leu Leu Arg Leu Gly Val Phe  
 85 90 95

35 Glu Ile Thr Ser Phe Asp Thr Pro Gln Leu Val Ala Val Asn Glu Ala  
 100 105 110

Ile Glu Leu Ala Lys Asp Phe Ser Asp Gln Lys Ser Ala Arg Phe Ile  
 115 120 125

40 Asn Gly Leu Leu Ser Gln Phe Val Thr Glu Glu Gln  
 130 135 140

45 <210> 219  
 <211> 1179  
 <212> PRT  
 <213> Streptococcus pneumoniae

50 <400> 219  
 Met Tyr Leu Lys Glu Ile Glu Ile Gln Gly Phe Lys Ser Phe Ala Asp  
 1 5 10 15

55 Lys Thr Lys Val Val Phe Asp Gln Gly Val Thr Ala Val Val Gly Pro  
 20 25 30

Asn Gly Ser Gly Lys Ser Asn Ile Thr Glu Ser Leu Arg Trp Ala Leu

|    | 35  | 40      | 45      |
|----|---|---------|---------|
|    | Gly Glu Ser Ser Val Lys Ser Leu Arg Gly Gly Lys Met Pro Asp Val |         |         |
|    | 50  | 55      | 60      |
| 5  | Ile Phe Ala Gly Thr Glu Ser Arg Lys Pro Leu Asn Tyr Ala Ser Val |         |         |
|    | 65  | 70      | 75 80   |
|    | Val Val Thr Leu Asp Asn His Asp Gly Phe Ile Lys Asp Ala Gly Gln |         |         |
| 10 |   | 85      | 90 95   |
|    | Glu Ile Arg Val Glu Arg His Ile Tyr Arg Ser Gly Asp Ser Glu Tyr |         |         |
|    | 100   | 105     | 110     |
| 15 | Lys Ile Asp Gly Lys Lys Val Arg Leu Arg Asp Ile His Asp Leu Phe |         |         |
|    | 115   | 120     | 125     |
|    | Leu Asp Thr Gly Leu Gly Arg Asp Ser Phe Ser Ile Ile Ser Gln Gly |         |         |
| 20 |   | 130 135 | 140     |
|    | Lys Val Glu Glu Ile Phe Asn Ser Lys Pro Glu Glu Arg Arg Ala Ile |         |         |
|    | 145   | 150     | 155 160 |
|    | Phe Glu Glu Ala Ala Gly Val Leu Lys Tyr Lys Thr Arg Arg Lys Glu |         |         |
| 25 |   | 165     | 170 175 |
|    | Thr Glu Ser Lys Leu Gln Gln Thr Gln Asp Asn Leu Asp Arg Leu Glu |         |         |
|    | 180   | 185     | 190     |
| 30 | Asp Ile Ile Tyr Glu Leu Asp Asn Gln Ile Lys Pro Leu Glu Lys Gln |         |         |
|    | 195   | 200     | 205     |
|    | Ala Glu Asn Ala Arg Lys Phe Leu Asp Leu Glu Gly Gln Arg Lys Ala |         |         |
| 35 |   | 210 215 | 220     |
|    | Ile Tyr Leu Asp Val Leu Val Ala Gln Ile Lys Glu Asn Lys Ala Glu |         |         |
|    | 225   | 230     | 235 240 |
|    | Leu Glu Ser Thr Glu Glu Glu Leu Ala Gln Val Gln Glu Leu Leu Met |         |         |
| 40 |   | 245     | 250 255 |
|    | Ser Tyr Tyr Gln Lys Arg Glu Lys Leu Glu Glu Glu Asn Gln Thr Leu |         |         |
|    | 260   | 265     | 270     |
| 45 | Lys Lys Gln Arg Gln Asp Leu Gln Ala Glu Met Ala Lys Asp Gln Gly |         |         |
|    | 275   | 280     | 285     |
|    | Ser Leu Met Asp Leu Thr Ser Leu Ile Ser Asp Leu Glu Arg Lys Leu |         |         |
| 50 |   | 290 295 | 300     |
|    | Ala Leu Ser Lys Leu Glu Ser Glu Gln Val Ala Leu Asn Gln Gln Glu |         |         |
|    | 305   | 310     | 315 320 |
|    | Ala Gln Ala Arg Leu Ala Ala Leu Glu Asp Lys Arg Asn Ser Leu Ser |         |         |
| 55 |   | 325     | 330 335 |
|    | Lys Glu Lys Tyr Asp Lys Glu Ser Ser Leu Ala Leu Leu Glu Gly Asn |         |         |

|    | 340   | 345                         | 350         |
|----|---|-----------------------------|-------------|
|    | Leu Val Gln Asn Asn Gln Lys                                     | Leu Asn Arg Leu Glu Ala     | Glu Leu Leu |
|    | 355   | 360                         | 365         |
| 5  | Ala Phe Ser Asp Asp Pro Asp                                     | Gln Met Ile Glu Leu Leu Arg | Glu Arg     |
|    | 370   | 375                         | 380         |
|    | Phe Val Ala Leu Leu Gln Glu Glu Ala Asp Val Ser Asn Gln Leu Thr |                             |             |
| 10 | 385   | 390                         | 395 400     |
|    | Arg Ile Glu Asn Glu Leu Glu Asn Ser Arg Gln Leu Ser Gln Lys Gln |                             |             |
|    | 405   | 410                         | 415         |
| 15 | Ala Asp Gln Leu Glu Lys Leu Lys Glu Gln Leu Ala Thr Ala Lys Glu |                             |             |
|    | 420   | 425                         | 430         |
|    | Lys Ala Ser Gln Gln Lys Asp Glu Leu Glu Thr Ala Lys Val Gln Val |                             |             |
| 20 | 435   | 440                         | 445         |
|    | Gln Lys Leu Leu Ala Asp Tyr Gln Ala Ile Ala Lys Glu Gln Glu Glu |                             |             |
|    | 450   | 455                         | 460         |
|    | Gln Lys Thr Ser Tyr Gln Ala Gln Gln Ser Gln Leu Phe Asp Arg Leu |                             |             |
| 25 | 465   | 470                         | 475 480     |
|    | Asp Ser Leu Lys Asn Lys Gln Ala Arg Ala Gln Ser Leu Glu Asn Ile |                             |             |
|    | 485   | 490                         | 495         |
| 30 | Leu Arg Asn His Ser Asn Phe Tyr Ala Gly Val Lys Ser Val Leu Gln |                             |             |
|    | 500   | 505                         | 510         |
|    | Glu Lys Asp Arg Leu Gly Gly Ile Ile Gly Ala Val Ser Glu His Leu |                             |             |
| 35 | 515   | 520                         | 525         |
|    | Thr Phe Asp Val Tyr Tyr Gln Thr Ala Leu Glu Ile Ala Leu Gly Ala |                             |             |
|    | 530   | 535                         | 540         |
|    | Ser Ser Gln His Ile Ile Val Glu Asp Glu Glu Ser Ala Thr Lys Ala |                             |             |
| 40 | 545   | 550                         | 555 560     |
|    | Ile Asp Phe Leu Lys Arg Asn Arg Val Gly Arg Ala Thr Phe Leu Pro |                             |             |
|    | 565   | 570                         | 575         |
| 45 | Leu Thr Thr Ile Lys Ala Arg Thr Ile Ser Ser Gln Asn Gln Asp Ala |                             |             |
|    | 580   | 585                         | 590         |
|    | Ile Ala Val Ser Pro Gly Phe Leu Gly Met Ala Asp Glu Leu Val Thr |                             |             |
| 50 | 595   | 600                         | 605         |
|    | Phe Asp Thr Arg Leu Glu Ala Ile Phe Lys Asn Leu Leu Ala Thr Thr |                             |             |
|    | 610   | 615                         | 620         |
|    | Ala Ile Phe Asp Thr Val Glu His Ala Arg Glu Ala Ala Arg Gln Val |                             |             |
| 55 | 625   | 630                         | 635 640     |
|    | Arg Tyr Gln Val Arg Met Val Thr Leu Asp Gly Thr Glu Leu Arg Thr |                             |             |

|    | 645   | 650 | 655 |
|----|---|-----|-----|
|    | Gly Gly Ser Tyr Ala Gly Gly Ala Asn Arg Gln Asn Asn Ser Ile Phe |     |     |
|    | 660   | 665 | 670 |
| 5  | Ile Lys Pro Glu Leu Glu Gln Leu Gln Lys Glu Ile Ala Ala Asp Glu |     |     |
|    | 675   | 680 | 685 |
|    | Ala Ser Leu Gly Ser Glu Glu Ala Ala Leu Lys Thr Leu Gln Asp Gln |     |     |
| 10 | 690   | 695 | 700 |
|    | Met Ala Ala Leu Thr Glu Arg Leu Glu Ala Ile Lys Ser Gln Gly Glu |     |     |
|    | 705   | 710 | 715 |
| 15 | Gln Ala Arg Ile Gln Glu Gln Gly Leu Ser Leu Ala Tyr Gln Gln Thr |     |     |
|    | 725   | 730 | 735 |
|    | Ser Gln Gln Val Glu Glu Leu Glu Thr Leu Trp Lys Leu Gln Glu Glu |     |     |
| 20 | 740   | 745 | 750 |
|    | Glu Ile Asp Arg Leu Ser Glu Gly Asp Trp Gln Ala Asp Lys Glu Lys |     |     |
|    | 755   | 760 | 765 |
|    | Cys Gln Glu Ser Leu Ala Thr Ile Ala Ser Asp Lys Gln Asn Leu Glu |     |     |
| 25 | 770   | 775 | 780 |
|    | Ala Glu Ile Glu Glu Ile Lys Ser Asn Lys Asn Ala Ile Gln Glu Arg |     |     |
|    | 785   | 790 | 795 |
| 30 | Tyr Gln Asn Leu Gln Glu Glu Val Ala Gln Ala Arg Leu Leu Lys Thr |     |     |
|    | 805   | 810 | 815 |
|    | Lys Leu Gln Gly Gln Lys Arg Tyr Glu Val Ala Asp Ile Glu Arg Leu |     |     |
| 35 | 820   | 825 | 830 |
|    | Gly Lys Glu Leu Asp Asn Leu Asn Ile Glu Gln Glu Glu Ile Gln Arg |     |     |
|    | 835   | 840 | 845 |
|    | Met Leu Gln Glu Lys Val Asp Asn Leu Glu Lys Val Asp Thr Glu Leu |     |     |
| 40 | 850   | 855 | 860 |
|    | Leu Ser Gln Gln Ala Glu Glu Ser Lys Thr Gln Lys Thr Asn Leu Gln |     |     |
|    | 865   | 870 | 875 |
| 45 | Gln Gly Leu Ile Arg Lys Gln Phe Glu Leu Asp Asp Ile Glu Gly Gln |     |     |
|    | 885   | 890 | 895 |
|    | Leu Asp Asp Ile Ala Ser His Leu Asp Gln Ala Arg Gln Gln Asn Glu |     |     |
| 50 | 900   | 905 | 910 |
|    | Glu Trp Ile Arg Lys Gln Thr Arg Ala Glu Ala Lys Lys Glu Lys Val |     |     |
|    | 915   | 920 | 925 |
|    | Ser Glu Arg Leu Arg His Leu Gln Asn Gln Leu Thr Asp Gln Tyr Gln |     |     |
| 55 | 930   | 935 | 940 |
|    | Ile Ser Tyr Thr Glu Ala Leu Glu Lys Ala His Glu Leu Glu Asn Leu |     |     |

|    |   |      |      |  |      |      |      |
|----|---|------|------|--|------|------|------|
|    | 945   |      | 950  |  | 955  |      | 960  |
|    | Asn Leu Ala Glu Gln Glu Val Gln Asp Leu Glu Lys Ala Ile Arg Ser |      |      |  |      |      |      |
|    |   | 965  |      |  | 970  |      | 975  |
| 5  | Leu Gly Pro Val Asn Leu Glu Ala Ile Asp Gln Tyr Glu Glu Val His |      |      |  |      |      |      |
|    |   | 980  |      |  | 985  |      | 990  |
| 10 | Asn Arg Leu Asp Phe Leu Asn Ser Gln Arg Asp Asp Ile Leu Ser Ala |      |      |  |      |      |      |
|    |   | 995  |      |  | 1000 |      | 1005 |
|    | Lys Asn Leu Leu Leu Glu Thr Ile Thr Glu Met Asn Asp Glu Val Lys |      |      |  |      |      |      |
|    |   | 1010 |      |  | 1015 |      | 1020 |
| 15 | Glu Arg Phe Lys Ser Thr Phe Glu Ala Ile Arg Glu Ser Phe Lys Val |      |      |  |      |      |      |
|    |   |      | 1030 |  |      | 1035 | 1040 |
|    | Thr Phe Lys Gln Met Phe Gly Gly Gly Gln Ala Asp Leu Ile Leu Thr |      |      |  |      |      |      |
|    |   |      | 1045 |  |      | 1050 | 1055 |
| 20 | Glu Gly Asp Leu Leu Thr Ala Gly Val Glu Ile Ser Val Gln Pro Pro |      |      |  |      |      |      |
|    |   | 1060 |      |  | 1065 |      | 1070 |
|    | Gly Lys Lys Ile Gln Ser Leu Asn Leu Met Ser Gly Gly Glu Lys Ala |      |      |  |      |      |      |
| 25 |   | 1075 |      |  | 1080 |      | 1085 |
|    | Leu Ser Ala Leu Ala Leu Leu Phe Ser Ile Ile Arg Val Lys Thr Ile |      |      |  |      |      |      |
|    |   | 1090 |      |  | 1095 |      | 1100 |
| 30 | Pro Phe Val Ile Leu Asp Glu Val Glu Ala Ala Leu Asp Glu Ala Asn |      |      |  |      |      |      |
|    |   |      | 1110 |  |      | 1115 | 1120 |
|    | Val Lys Arg Phe Gly Asp Tyr Leu Asn Arg Phe Asp Lys Asp Ser Gln |      |      |  |      |      |      |
|    |   |      | 1125 |  |      | 1130 | 1135 |
| 35 | Phe Ile Val Val Thr His Arg Lys Gly Thr Met Ala Ala Ala Asp Ser |      |      |  |      |      |      |
|    |   | 1140 |      |  |      | 1145 | 1150 |
|    | Ile Tyr Gly Val Thr Met Gln Glu Ser Gly Val Ser Lys Ile Val Ser |      |      |  |      |      |      |
| 40 |   | 1155 |      |  | 1160 |      | 1165 |
|    | Val Lys Leu Lys Asp Leu Glu Ser Ile Glu Gly                     |      |      |  |      |      |      |
|    |   | 1170 |      |  | 1175 |      |      |
| 45 | <210> 220   |      |      |  |      |      |      |
|    | <211> 447   |      |      |  |      |      |      |
|    | <212> PRT   |      |      |  |      |      |      |
|    | <213> Streptococcus pneumoniae                                  |      |      |  |      |      |      |
| 50 | <400> 220   |      |      |  |      |      |      |
|    | Met Thr Lys Arg Val Thr Ile Ile Asp Val Lys Asp Tyr Val Gly Gln |      |      |  |      |      |      |
|    | 1   |      | 5    |  |      | 10   | 15   |
| 55 | Glu Val Thr Ile Gly Ala Trp Val Ala Asn Lys Ser Gly Lys Gly Lys |      |      |  |      |      |      |
|    |   | 20   |      |  |      | 25   | 30   |

Ile Ala Phe Leu Gln Leu Arg Asp Gly Thr Ala Phe Phe Gln Gly Val  
                   35                                  40                                  45  
 5 Ala Phe Lys Pro Asn Phe Val Glu Lys Phe Gly Glu Glu Val Gly Leu  
                   50                                  55                                  60  
 Glu Lys Phe Asp Val Ile Lys Arg Leu Ser Gln Glu Thr Ser Val Tyr  
                   65                                  70                                  75                                  80  
 10 Val Thr Gly Ile Val Lys Glu Asp Glu Arg Ser Lys Phe Gly Tyr Glu  
                                   85                                  90                                  95  
 Leu Asp Ile Thr Asp Ile Glu Val Ile Gly Glu Ser Gln Asp Tyr Pro  
                                   100                                  105                                  110  
 15 Ile Thr Pro Lys Glu His Gly Thr Asp Phe Leu Met Asp Asn Arg His  
                                   115                                  120                                  125  
 Leu Trp Leu Arg Ser Arg Lys Gln Val Ala Val Leu Gln Ile Arg Asn  
                   130                                  135                                  140  
 Ala Ile Ile Tyr Ala Thr Tyr Glu Phe Phe Asp Lys Asn Gly Phe Met  
                   145                                  150                                  155                                  160  
 25 Lys Phe Asp Ser Pro Ile Leu Ser Gly Asn Ala Ala Glu Asp Ser Thr  
                                   165                                  170                                  175  
 Glu Leu Phe Glu Thr Asp Tyr Phe Gly Thr Pro Ala Tyr Leu Ser Gln  
                                   180                                  185                                  190  
 30 Ser Gly Gln Leu Tyr Leu Glu Ala Gly Ala Met Ala Leu Gly Arg Val  
                                   195                                  200                                  205  
 Phe Asp Phe Gly Pro Val Phe Arg Ala Glu Lys Ser Lys Thr Arg Arg  
                   210                                  215                                  220  
 His Leu Thr Glu Phe Trp Met Met Asp Ala Glu Tyr Ser Tyr Leu Thr  
                   225                                  230                                  235                                  240  
 40 His Asp Glu Ser Leu Asp Leu Gln Glu Ala Tyr Val Lys Ala Leu Leu  
                                   245                                  250                                  255  
 Gln Gly Val Leu Asp Arg Ala Pro Gln Ala Leu Glu Thr Leu Glu Arg  
                                   260                                  265                                  270  
 45 Asp Thr Glu Leu Leu Lys Arg Tyr Ile Ala Glu Pro Phe Lys Arg Ile  
                                   275                                  280                                  285  
 Thr Tyr Asp Gln Ala Ile Asp Leu Leu Gln Glu His Glu Asn Asp Glu  
                   290                                  295                                  300  
 Asp Ala Asp Tyr Glu His Leu Glu His Gly Asp Asp Phe Gly Ser Pro  
                   305                                  310                                  315                                  320  
 55 His Glu Thr Trp Ile Ser Asn His Phe Gly Val Pro Thr Phe Val Met  
                                   325                                  330                                  335

Asn Tyr Pro Ala Ala Ile Lys Ala Phe Tyr Met Lys Pro Val Pro Gly  
 340 345 350  
 5 Asn Pro Glu Arg Val Leu Cys Ala Asp Leu Leu Ala Pro Glu Gly Tyr  
 355 360 365  
 Gly Glu Ile Ile Gly Gly Ser Met Arg Glu Glu Asp Tyr Asp Ala Leu  
 370 375 380  
 10 Val Ala Lys Met Asp Glu Leu Gly Met Asp Arg Thr Glu Tyr Glu Phe  
 385 390 395 400  
 Tyr Leu Asp Leu Arg Lys Tyr Gly Thr Val Pro His Gly Gly Phe Gly  
 405 410 415  
 15 Ile Gly Ile Glu Arg Met Val Thr Phe Ala Ala Gly Thr Lys His Ile  
 420 425 430  
 20 Arg Glu Ala Ile Pro Phe Pro Arg Met Leu His Arg Ile Lys Pro  
 435 440 445  
 <210> 221  
 <211> 308  
 25 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 221  
 30 Met Ser Glu Lys Leu Val Glu Ile Lys Asp Leu Glu Ile Ser Phe Gly  
 1 5 10 15  
 Glu Gly Ser Lys Lys Phe Val Ala Val Lys Asn Ala Asn Phe Phe Ile  
 20 25 30  
 35 Asn Lys Gly Glu Thr Phe Ser Leu Val Gly Glu Ser Gly Ser Gly Lys  
 35 40 45  
 Thr Thr Ile Gly Arg Ala Ile Ile Gly Leu Asn Asp Thr Ser Asn Gly  
 50 55 60  
 40 Asp Ile Ile Phe Asp Gly Gln Lys Ile Asn Gly Lys Lys Ser Arg Glu  
 65 70 75 80  
 Gln Ala Ala Glu Leu Ile Arg Arg Ile Gln Met Ile Phe Gln Asp Pro  
 85 90 95  
 45 Ala Ala Ser Leu Asn Glu Arg Ala Thr Val Asp Tyr Ile Ile Ser Glu  
 100 105 110  
 50 Gly Leu Tyr Asn His Arg Leu Phe Lys Asp Glu Glu Glu Arg Lys Glu  
 115 120 125  
 Lys Val Gln Asn Ile Ile Arg Glu Val Gly Leu Leu Ala Glu His Leu  
 130 135 140  
 55 Thr Arg Tyr Pro His Glu Phe Ser Gly Gly Gln Arg Gln Arg Ile Gly  
 145 150 155 160

Ile Ala Arg Ala Leu Val Met Gln Pro Asp Phe Val Ile Ala Asp Glu  
 165 170 175  
 5 Pro Ile Ser Ala Leu Asp Val Ser Val Arg Ala Gln Val Leu Asn Leu  
 180 185 190  
 Leu Lys Lys Phe Gln Lys Glu Leu Gly Leu Thr Tyr Leu Phe Ile Ala  
 195 200 205  
 10 His Asp Leu Ser Val Val Arg Phe Ile Ser Asp Arg Ile Ala Val Ile  
 210 215 220  
 Tyr Lys Gly Val Ile Val Glu Val Ala Glu Thr Glu Glu Leu Phe Asn  
 15 225 230 235 240  
 Asn Pro Ile His Pro Tyr Thr Gln Ala Leu Leu Ser Ala Val Pro Ile  
 245 250 255  
 20 Pro Asp Pro Ile Leu Glu Arg Lys Lys Val Leu Lys Val Tyr Asp Pro  
 260 265 270  
 Ser Gln His Asp Tyr Glu Thr Asp Lys Pro Ser Met Val Glu Ile Arg  
 275 280 285  
 25 Pro Gly His Tyr Val Trp Ala Asn Gln Thr Glu Leu Ala Arg Tyr Gln  
 290 295 300  
 Lys Gly Leu Asn  
 30 305  
 <210> 222  
 <211> 424  
 35 <212> PRT  
 <213> Streptococcus pneumoniae  
 <400> 222  
 40 Met Lys Ile Ser Trp Asn Gly Phe Ser Lys Lys Ser Tyr Gln Glu Arg  
 1 5 10 15  
 Leu Glu Leu Leu Lys Ala Gln Ala Leu Leu Ser Pro Glu Arg Gln Ala  
 20 25 30  
 45 Ser Leu Glu Lys Asp Glu Gln Met Ser Val Thr Val Ala Asp Gln Leu  
 35 40 45  
 Ser Glu Asn Val Val Gly Thr Phe Ser Leu Pro Tyr Ser Leu Val Pro  
 50 50 55 60  
 Glu Val Leu Val Asn Gly Gln Glu Tyr Thr Val Pro Tyr Val Thr Glu  
 55 65 70 75 80  
 Glu Pro Ser Val Val Ala Ala Ala Ser Tyr Ala Ser Lys Ile Ile Lys  
 85 90 95  
 Arg Ala Gly Gly Phe Thr Ala Gln Val His Gln Arg Gln Met Ile Gly



|    | 100   | 105 | 110 |
|----|---|-----|-----|
|    | Gln Val Ala Leu Tyr Gln Ile Ala Asn Pro Lys Leu Ala Gln Glu Lys |     |     |
|    | 115   | 120 | 125 |
| 5  | Ile Ala Ser Lys Lys Ala Glu Leu Leu Glu Leu Ala Asn Gln Ala Tyr |     |     |
|    | 130   | 135 | 140 |
| 10 | Pro Ser Ile Val Lys Arg Gly Gly Gly Ala Arg Asp Leu His Val Glu |     |     |
|    | 145   | 150 | 155 |
|    | Gln Ile Lys Gly Glu Pro Asp Phe Leu Val Val Tyr Ile His Val Asp |     |     |
|    | 165   | 170 | 175 |
| 15 | Thr Gln Glu Ala Met Gly Ala Asn Met Leu Asn Thr Met Leu Glu Ala |     |     |
|    | 180   | 185 | 190 |
|    | Leu Lys Pro Val Leu Glu Glu Leu Ser Gln Gly Gln Ser Leu Met Gly |     |     |
|    | 195   | 200 | 205 |
| 20 | Ile Leu Ser Asn Tyr Ala Thr Asp Ser Leu Val Thr Ala Ser Cys Arg |     |     |
|    | 210   | 215 | 220 |
| 25 | Ile Ala Phe Arg Tyr Leu Ser Arg Gln Lys Asp Gln Gly Arg Glu Ile |     |     |
|    | 225   | 230 | 235 |
|    | Ala Glu Lys Ile Ala Leu Ala Ser Gln Phe Ala Gln Ala Asp Pro Tyr |     |     |
|    | 245   | 250 | 255 |
| 30 | Arg Ala Ala Thr His Asn Lys Gly Ile Phe Asn Gly Ile Asp Ala Ile |     |     |
|    | 260   | 265 | 270 |
|    | Leu Ile Ala Thr Gly Asn Asp Trp Arg Ala Ile Glu Ala Gly Ala His |     |     |
|    | 275   | 280 | 285 |
| 35 | Ala Phe Ala Ser Arg Asp Gly Arg Tyr Gln Gly Leu Ser Cys Trp Thr |     |     |
|    | 290   | 295 | 300 |
| 40 | Leu Asp Leu Glu Arg Glu Glu Leu Val Gly Glu Met Thr Leu Pro Met |     |     |
|    | 305   | 310 | 315 |
|    | Pro Val Ala Thr Lys Gly Gly Ser Ile Gly Leu Asn Pro Arg Val Ala |     |     |
|    | 325   | 330 | 335 |
| 45 | Leu Ser His Asp Leu Leu Gly Asn Pro Ser Ala Arg Glu Leu Ala Gln |     |     |
|    | 340   | 345 | 350 |
|    | Ile Ile Val Ser Ile Gly Leu Ala Gln Asn Phe Ala Ala Leu Lys Ala |     |     |
|    | 355   | 360 | 365 |
| 50 | Leu Val Ser Thr Gly Ile Gln Gln Gly His Met Lys Leu Gln Ala Lys |     |     |
|    | 370   | 375 | 380 |
| 55 | Ser Leu Ala Leu Leu Ala Gly Ala Ser Glu Ser Glu Val Ala Pro Leu |     |     |
|    | 385   | 390 | 395 |
|    | Val Glu Arg Leu Ile Ser Asp Lys Thr Phe Asn Leu Glu Thr Ala Gln |     |     |

405 410 415

Arg Tyr Leu Glu Asn Leu Arg Ser  
420

5

<210> 223  
<211> 262  
<212> PRT  
10 <213> Streptococcus pneumoniae

<400> 223  
Met Pro Ile Thr Ser Leu Glu Ile Lys Asp Lys Thr Phe Gly Thr Arg  
1 5 10 15

15 Phe Arg Gly Phe Asp Pro Glu Glu Val Asp Glu Phe Leu Asp Ile Val  
20 25 30

20 Val Arg Asp Tyr Glu Asp Leu Val Arg Ala Asn His Asp Lys Asn Leu  
35 40 45

Arg Ile Lys Ser Leu Glu Glu Arg Leu Ser Tyr Phe Asp Glu Ile Lys  
50 55 60

25 Asp Ser Leu Ser Gln Ser Val Leu Ile Ala Gln Asp Thr Ala Glu Arg  
65 70 75 80

Val Lys Gln Ala Ala His Glu Arg Ser Asn Asn Ile Ile His Gln Ala  
85 90 95

30 Glu Gln Asp Ala Gln Arg Leu Leu Glu Glu Ala Lys Tyr Lys Ala Asn  
100 105 110

35 Glu Ile Leu Arg Gln Ala Thr Asp Asn Ala Lys Lys Val Ala Val Glu  
115 120 125

Thr Glu Glu Leu Lys Asn Lys Ser Arg Val Phe His Gln Arg Leu Lys  
130 135 140

40 Ser Thr Ile Glu Ser Gln Leu Ala Ile Val Glu Ser Ser Asp Trp Glu  
145 150 155 160

Asp Ile Leu Arg Pro Thr Ala Thr Tyr Leu Gln Thr Ser Asp Glu Ala  
165 170 175

45 Phe Lys Glu Val Val Ser Glu Val Leu Gly Glu Pro Ile Pro Ala Pro  
180 185 190

Ile Glu Glu Glu Pro Ile Asp Met Thr Arg Gln Phe Ser Gln Ala Glu  
195 200 205

50 Met Ala Glu Leu Gln Ala Arg Ile Glu Val Ala Asp Lys Glu Leu Ser  
210 215 220

55 Glu Phe Glu Ala Gln Ile Lys Gln Glu Val Glu Ala Pro Thr Pro Val  
225 230 235 240

Val Ser Pro Gln Val Glu Glu Glu Pro Leu Leu Ile Gln Leu Ala Gln  
245 250 255

5 Cys Met Lys Asn Gln Lys  
260

10 <210> 224  
<211> 575  
<212> PRT  
<213> Streptococcus pneumoniae

15 <400> 224  
Met Ser Asn Gly Gln Leu Ile Tyr Leu Met Val Ala Ile Ala Val Ile  
1 5 10 15

Leu Val Leu Ala Tyr Val Val Ala Ile Phe Leu Arg Lys Arg Asn Glu  
20 20 25 30

20 Gly Arg Leu Glu Ala Leu Glu Glu Arg Lys Glu Glu Leu Tyr Asn Leu  
35 40 45

Pro Val Asn Asp Glu Val Glu Ala Val Lys Asn Met His Leu Ile Gly  
25 50 55 60

25 Gln Ser Gln Val Ala Phe Arg Glu Trp Asn Gln Lys Trp Val Asp Leu  
65 70 75 80

30 Ser Leu Asn Ser Phe Ala Asp Ile Glu Asn Asn Leu Phe Glu Ala Glu  
85 90 95

Gly Tyr Asn His Ser Phe Arg Phe Leu Lys Ala Ser His Gln Ile Asp  
100 105 110

35 Gln Ile Glu Ser Gln Ile Thr Leu Ile Glu Glu Asp Ile Ala Ala Ile  
115 120 125

Arg Asn Ala Leu Ala Asp Leu Glu Lys Gln Glu Ser Lys Asn Ser Gly  
40 130 135 140

40 Arg Val Leu His Ala Leu Asp Leu Phe Glu Glu Leu Gln His Arg Val  
145 150 155 160

45 Ala Glu Asn Ser Glu Gln Tyr Gly Gln Ala Leu Asp Glu Ile Glu Lys  
165 170 175

Gln Leu Glu Asn Ile Gln Ser Glu Phe Ser Gln Phe Val Thr Leu Asn  
180 185 190

50 Ser Ser Gly Asp Pro Val Glu Ala Ala Val Ile Leu Asp Asn Thr Glu  
195 200 205

Asn His Ile Leu Ala Leu Ser His Ile Val Asp Arg Val Pro Ala Leu  
210 215 220

55 Val Thr Thr Leu Ser Thr Glu Leu Pro Asp Gln Leu Gln Asp Leu Glu  
225 230 235 240

Ala Gly Tyr Arg Lys Leu Ile Asp Ala Asn Tyr His Phe Val Glu Thr  
 245 250 255  
 5 Asp Ile Glu Ala Arg Phe His Leu Leu Tyr Glu Ala Phe Lys Lys Asn  
 260 265 270  
 Gln Glu Asn Ile Arg Gln Leu Glu Leu Asp Asn Ala Glu Tyr Glu Asn  
 275 280 285  
 10 Gly Gln Ala Gln Glu Glu Ile Asn Ala Leu Tyr Asp Ile Phe Thr Arg  
 290 295 300  
 Glu Ile Ala Ala Gln Lys Val Val Glu Asn Leu Leu Ala Thr Leu Pro  
 15 305 310 315 320  
 Thr Tyr Leu Gln His Met Lys Glu Asn Asn Thr Leu Leu Gly Glu Asp  
 325 330 335  
 20 Ile Ala Arg Leu Asn Lys Thr Tyr Leu Leu Pro Glu Thr Ala Ala Ser  
 340 345 350  
 His Val Arg Arg Ile Gln Thr Glu Leu Glu Ser Phe Glu Ala Ala Ile  
 355 360 365  
 25 Val Glu Val Thr Ser Asn Gln Glu Glu Pro Thr Gln Ala Tyr Ser Val  
 370 375 380  
 Leu Glu Glu Asn Leu Glu Asp Leu Gln Thr Gln Leu Lys Asp Ile Glu  
 30 385 390 395 400  
 Asp Glu Gln Ile Ser Val Ser Glu Arg Leu Thr Gln Ile Glu Lys Asp  
 405 410 415  
 35 Asp Ile Asn Ala Arg Gln Lys Ala Asn Val Tyr Val Asn Arg Leu His  
 420 425 430  
 Thr Ile Lys Arg Tyr Met Glu Lys Arg Asn Leu Pro Gly Ile Pro Gln  
 435 440 445  
 40 Thr Phe Leu Lys Leu Phe Phe Thr Ala Ser Asn Asn Thr Glu Asp Leu  
 450 455 460  
 Met Val Glu Leu Glu Gln Lys Met Ile Asn Ile Glu Ser Val Thr Arg  
 45 465 470 475 480  
 Val Leu Glu Ile Ala Thr Asn Asp Met Glu Ala Leu Glu Thr Glu Thr  
 485 490 495  
 50 Tyr Asn Ile Val Gln Tyr Ala Thr Leu Thr Glu Gln Leu Leu Gln Tyr  
 500 505 510  
 Ser Asn Arg Tyr Arg Ser Phe Asp Glu Arg Ile Gln Glu Ala Phe Asn  
 515 520 525  
 55 Glu Ala Leu Asp Ile Phe Glu Lys Glu Phe Asp Tyr His Ala Ser Phe  
 530 535 540

Asp Lys Ile Ser Gln Ala Leu Glu Val Ala Glu Pro Gly Val Thr Asn  
 545 550 555 560

5 Arg Phe Val Thr Ser Tyr Glu Lys Thr Arg Glu Thr Ile Arg Phe  
 565 570 575

<210> 225  
 10 <211> 800  
 <212> PRT  
 <213> Streptococcus pneumoniae

<400> 225  
 15 Met Leu Ile Ser Tyr Lys Trp Leu Lys Glu Leu Val Asp Ile Asp Val  
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Pro Ser Gln Glu Leu Ala Glu Lys Met Ser Thr Thr Gly Ile Glu Val  
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Glu Gly Val Glu Ser Pro Ala Ala Gly Leu Ser Lys Ile Val Val Gly  
 35 40 45

Glu Val Leu Ser Cys Glu Asp Val Pro Glu Thr His Leu His Val Cys  
 25 50 55 60

Gln Val Asn Val Gly Glu Glu Glu Arg Gln Ile Val Cys Gly Ala Pro  
 65 70 75 80

30 Asn Val Arg Ala Gly Ile Lys Val Met Val Ala Leu Pro Gly Ala Arg  
 85 90 95

Ile Ala Asp Asn Tyr Lys Ile Lys Lys Gly Lys Ile Arg Gly Leu Glu  
 100 105 110

35 Ser Leu Gly Met Ile Cys Ser Leu Gly Glu Leu Gly Ile Ser Asp Ser  
 115 120 125

Val Val Pro Lys Glu Phe Ala Asp Gly Ile Gln Ile Leu Pro Glu Asp  
 40 130 135 140

Ala Val Pro Gly Glu Glu Val Phe Ser Tyr Leu Asp Leu Asp Asp Glu  
 145 150 155 160

45 Ile Ile Glu Leu Ser Ile Thr Pro Asn Arg Ala Asp Ala Leu Ser Met  
 165 170 175

Cys Gly Val Ala His Glu Val Ala Ala Ile Tyr Asp Lys Ala Val Asn  
 180 185 190

50 Phe Lys Glu Phe Thr Leu Thr Glu Thr Asn Glu Ala Ala Ala Asp Ala  
 195 200 205

Leu Ser Val Ser Ile Glu Thr Asp Lys Ala Pro Tyr Tyr Ala Ala Arg  
 55 210 215 220

Ile Leu Asp Asn Val Thr Ile Ala Pro Ser Pro Gln Trp Leu Gln Asn

|    |   |     |     |     |     |  |     |
|----|---|-----|-----|-----|-----|--|-----|
|    | 225   |     | 230 |     | 235 |  | 240 |
|    | Leu Leu Met Asn Glu Gly Ile Arg Pro Ile Asn Asn Val Val Asp Val |     |     |     |     |  |     |
|    |   | 245 |     |     | 250 |  | 255 |
| 5  | Thr Asn Tyr Ile Leu Leu Tyr Phe Gly Gln Pro Met His Ala Phe Asp |     |     |     |     |  |     |
|    |   | 260 |     | 265 |     |  | 270 |
| 10 | Leu Asp Asn Phe Glu Gly Thr Asp Ile Arg Val Arg Glu Ala Arg Ala |     |     |     |     |  |     |
|    |   | 275 |     | 280 |     |  | 285 |
|    | Gly Glu Lys Leu Val Thr Leu Asp Gly Glu Glu Arg Asp Leu Asp Val |     |     |     |     |  |     |
|    |   | 290 |     | 295 |     |  | 300 |
| 15 | Asn Asp Leu Val Ile Thr Val Ala Asp Lys Pro Val Ala Leu Ala Gly |     |     |     |     |  |     |
|    |   | 305 |     | 310 |     |  | 315 |
|    | Val Met Gly Gly Gln Ala Thr Glu Ile Ser Glu Lys Ser Ser Arg Val |     |     |     |     |  |     |
|    |   |     | 325 |     | 330 |  | 335 |
| 20 | Val Leu Glu Ala Ala Val Phe Asn Gly Lys Ser Ile Arg Lys Thr Ser |     |     |     |     |  |     |
|    |   | 340 |     | 345 |     |  | 350 |
|    | Gly Arg Leu Asn Leu Arg Ser Glu Ser Ser Ser Arg Phe Glu Lys Gly |     |     |     |     |  |     |
| 25 |   | 355 |     | 360 |     |  | 365 |
|    | Ile Asn Val Ala Thr Val Asn Glu Ala Leu Asp Ala Ala Ala Ser Leu |     |     |     |     |  |     |
|    |   | 370 |     | 375 |     |  | 380 |
| 30 | Ile Ala Glu Leu Ala Gly Ala Thr Val Arg Lys Gly Ile Val Ser Ala |     |     |     |     |  |     |
|    |   | 385 |     | 390 |     |  | 395 |
|    | Gly Glu Leu Asp Thr Ser Asp Val Glu Val Ser Ser Thr Leu Ala Asp |     |     |     |     |  |     |
|    |   | 405 |     | 410 |     |  | 415 |
| 35 | Val Asn Arg Val Leu Gly Thr Glu Leu Ser Tyr Ala Asp Val Glu Asp |     |     |     |     |  |     |
|    |   | 420 |     | 425 |     |  | 430 |
|    | Val Phe Arg Arg Leu Gly Phe Gly Leu Ser Gly Asn Ala Asp Ser Phe |     |     |     |     |  |     |
| 40 |   | 435 |     | 440 |     |  | 445 |
|    | Thr Val Arg Val Pro Arg Arg Arg Trp Asp Ile Thr Ile Glu Ala Asp |     |     |     |     |  |     |
|    |   | 450 |     | 455 |     |  | 460 |
| 45 | Leu Phe Glu Glu Ile Ala Arg Ile Tyr Gly Tyr Asp Arg Leu Pro Thr |     |     |     |     |  |     |
|    |   | 465 |     | 470 |     |  | 475 |
|    | Ser Leu Pro Lys Asp Asp Gly Thr Ala Gly Glu Leu Thr Ala Thr Gln |     |     |     |     |  |     |
|    |   | 485 |     | 490 |     |  | 495 |
| 50 | Lys Leu Arg Arg Gln Val Arg Thr Ile Ala Glu Gly Ala Gly Leu Thr |     |     |     |     |  |     |
|    |   | 500 |     | 505 |     |  | 510 |
|    | Glu Ile Ile Thr Tyr Thr Leu Thr Thr Pro Glu Lys Ala Val Glu Phe |     |     |     |     |  |     |
| 55 |   | 515 |     | 520 |     |  | 525 |
|    | Thr Ala Gln Pro Ser Asn Leu Thr Glu Leu Met Trp Pro Met Thr Val |     |     |     |     |  |     |

|    | 530   | 535     | 540     |
|----|---|---------|---------|
|    | Asp Arg Ser Val Leu Arg Gln Asn Met Ile Ser Gly Ile Leu Asp Thr |         |         |
|    | 545   | 550     | 555 560 |
| 5  | Val Ala Tyr Asn Val Ala Arg Lys Asn Lys Asn Leu Ala Leu Tyr Glu |         |         |
|    |   | 565     | 570 575 |
|    | Ile Gly Lys Val Phe Glu Gln Thr Gly Asn Pro Lys Glu Glu Leu Pro |         |         |
| 10 |   | 580     | 585 590 |
|    | Asn Glu Ile Asn Ser Phe Ala Phe Ala Leu Thr Gly Leu Val Ala Glu |         |         |
|    |   | 595     | 600 605 |
| 15 | Lys Asp Phe Gln Thr Ala Ala Val Pro Val Asp Phe Phe Tyr Ala Lys |         |         |
|    |   | 610 615 | 620     |
|    | Gly Ile Leu Glu Ala Leu Phe Thr Arg Leu Gly Leu Gln Val Thr Tyr |         |         |
| 20 |   | 625 630 | 635 640 |
|    | Thr Ala Thr Ser Glu Ile Ala Ser Leu His Pro Gly Arg Thr Ala Val |         |         |
|    |   | 645     | 650 655 |
|    | Ile Ser Leu Gly Asp Gln Val Leu Gly Phe Leu Gly Gln Val His Pro |         |         |
| 25 |   | 660     | 665 670 |
|    | Val Thr Ala Lys Ala Tyr Asp Ile Pro Glu Thr Tyr Val Ala Glu Leu |         |         |
|    |   | 675     | 680 685 |
| 30 | Asn Leu Ser Ala Ile Glu Ala Ala Leu Gln Pro Ala Thr Pro Phe Val |         |         |
|    |   | 690 695 | 700     |
|    | Glu Ile Thr Lys Phe Pro Ala Val Ser Arg Asp Val Ala Leu Leu Leu |         |         |
| 35 |   | 705 710 | 715 720 |
|    | Lys Ala Glu Val Thr His Gln Glu Val Val Asp Ala Ile Gln Ala Ala |         |         |
|    |   | 725     | 730 735 |
|    | Gly Val Lys Arg Leu Thr Asp Ile Lys Leu Phe Asp Val Phe Ser Gly |         |         |
| 40 |   | 740     | 745 750 |
|    | Glu Lys Leu Gly Leu Gly Met Lys Ser Met Ala Tyr Ser Leu Thr Phe |         |         |
|    |   | 755     | 760 765 |
| 45 | Gln Asn Pro Glu Asp Ser Leu Thr Asp Glu Glu Val Ala Arg Tyr Met |         |         |
|    |   | 770 775 | 780     |
|    | Glu Lys Ile Gln Ala Ser Leu Glu Glu Lys Val Asn Ala Glu Val Arg |         |         |
| 50 |   | 785 790 | 795 800 |
| 55 | <210> 226   |         |         |
|    | <211> 180   |         |         |
|    | <212> PRT   |         |         |

&lt;213&gt; Streptococcus pneumoniae

&lt;400&gt; 226

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5   Met Leu Glu Asn Asp Ile Lys Lys Val Leu Val Ser His Asp Glu Ile
    1           5           10           15

    Thr Glu Ala Ala Lys Lys Leu Gly Ala Gln Leu Thr Lys Asp Tyr Ala
           20           25           30

10  Gly Lys Asn Pro Ile Leu Val Gly Ile Leu Lys Gly Ser Ile Pro Phe
           35           40           45

    Met Ala Glu Leu Val Lys His Ile Asp Thr His Ile Glu Met Asp Phe
           50           55           60

15  Met Met Val Ser Ser Tyr His Gly Gly Thr Ala Ser Ser Gly Val Ile
    65           70           75           80

    Asn Ile Lys Gln Asp Val Thr Gln Asp Ile Lys Gly Arg His Val Leu
    85           90           95

    Phe Val Glu Asp Ile Ile Asp Thr Gly Gln Thr Leu Lys Asn Leu Arg
           100           105           110

25  Asp Met Phe Lys Ala Arg Glu Ala Ala Ser Val Lys Ile Ala Thr Leu
    115           120           125

    Leu Asp Lys Pro Glu Gly Arg Val Val Glu Ile Glu Ala Asp Tyr Thr
    130           135           140

30  Cys Phe Thr Ile Pro Asn Glu Phe Val Val Gly Tyr Gly Leu Asp Tyr
    145           150           155           160

    Lys Glu Asn Tyr Arg Asn Leu Pro Tyr Ile Gly Val Leu Lys Glu Glu
    165           170           175

    Val Tyr Ser Asn
           180

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